
APASL Oncology 2024 Chiba
Chiba Prefecture Mascot CHI-BA-KUN
千葉県許諾第2754-2号
The Asian Pacific Association for the Study of the Liver
Asian Pacific Association for the Study of the Liver
APASL Oncology 2024
Genomics Meets Immunology :
Interdisciplinary Approach for Liver Cancer
Program & Abstracts
Term: September 24-25, 2024
City: Chiba, Japan
Venue: Sheraton Grande Tokyo Bay Hotel
President: Naoya Kato M.D., Ph.D.
Professor, Department of Gastroenterology
Graduate School of Medicine, Chiba University
www.apasl-oncology2024.org
Supported by JSH

abbvie

Raising a smile for tomorrow, together.

There are people living with illness,
people fighting pain.
And then there are people
who walk beside them, offering care.
Each with their own anxieties and worries,
they' re feeling their way through the dark.
At AbbVie, we aspire to light
a beacon of hope in these lives.

Our diverse team has always been,
and continues to be
united in creating new medicines
and healthcare approaches
through world-class science,
working to seek new solutions for patients.

And looking ahead,
to make the tomorrow we hope for even brighter,
AbbVie will work hand in hand with people
who share our aspirations.
Doing our part to serve
and support our communities
and protect the environment,
making a lasting impact
that's felt within healthcare and beyond.

So that everyone in society
can live true to themselves
with a smile on their face.

AbbVie GK
3-1-21 Shibaura, Minato-ku
Tokyo 108-0023, Japan
https://www.abbvie.co.jp/

People. Passion.
Possibilities.®

すべての革新は患者さんのために

CHUGAI 中外製薬

Roche ロシュ グループ

遺伝子パネル検査を、もっと日本のがん患者さんへ。

TISSUE：組織検体

FOUNDATIONONE®CDx
がんゲノムプロファイル

LIQUID：血液検体

FOUNDATIONONE®LIQUID CDx
がんゲノムプロファイル

高度管理医療機器　遺伝子変異解析プログラム（がんゲノムプロファイリング検査用）　体細胞遺伝子変異解析プログラム（抗悪性腫瘍薬適応判定用）

FoundationOne® CDx がんゲノムプロファイル　承認番号：23000BZX00403000

FoundationOne® Liquid CDx がんゲノムプロファイル　承認番号：30300BZX00074000

使用目的又は効果、使用方法、注意事項等情報等につきましては、電子化された添付文書情報をご参照ください。

2023年3月作成

製造販売元　CHUGAI 中外製薬株式会社
〒103-8324 東京都中央区日本橋室町2-1-1
Roche ロシュ グループ
〔文献請求先及び問い合わせ先〕メディカルインフォメーション部
TEL.0120-189-706　FAX.0120-189-705
〔販売情報提供活動に関する問い合わせ先〕
https://www.chugai-pharm.co.jp/guideline/

APASL Oncology 2024 Chiba

"Genomics Meets Immunology: Interdisciplinary Approach for Liver Cancer"

September 24-25, 2024

Table of Contents

Welcome Message

Dear Colleagues,

On behalf of the Organizing Committee, it gives us great pleasure to welcome you to the Asian Pacific Association for the Study of the Liver (APASL) Oncology 2024 Chiba, which will be held on September 24-25, 2024 in Chiba, Japan.

The scientific program will consist of invited lectures, symposia, plenary session, and poster sessions on the theme of "Genomics Meets Immunology: Interdisciplinary Approach for Liver Cancer". The program will provide the latest information and fresh ideas for hepatologists.

Talking about the history of us, one of the founding fathers of APASL, Dr. Kunio Okuda, taught at our department, and he had accepted many international students who have been prominent hepatologists and now active leaders of hepatology in their own countries. Today, following in the footsteps of our predecessors, we are continuing to conduct significant researches and activities.

The conference encouraged the submission of abstracts on research for oral and poster presentations and received more than 170 free papers. We would appreciate your submission which will stimulate active discussions.

The delegates of experts from all over the world are expected to attend this conference. We are sure that this will provide an excellent opportunity for those of us in the Asian Pacific region to share the latest views, values, experience and practice, and greatly contribute to this field.

We are looking forward to welcoming you to the beautiful venue with pleasant ocean breeze.

With warmest regards,

Naoya Kato, MD, PhD
President of APASL Oncology 2024 Chiba
Professor, Department of Gastroenterology
Graduate School of Medicine, Chiba University

Invited Guest Speakers/Chairs/Scientific Committee

Invited Guests/Speakers/Chairs/Scientific Committee from Overseas

Dr. Oidov Baatarkhuu (Mongolia)
Dr. Stephen Lam Chan (Hong Kong)
Dr. A. Kadir Dokmeci (Turkey)
Dr. Rino Gani (Indonesia)
Dr. Yujin Hoshida (USA)
Dr. Yi-Hsiang Huang (Taiwan)
Dr. Amarsanaa Jazag (Mongolia)
Dr. George K. K. Lau (Hong Kong)
Dr. Diana A. Payawal (Philippines)
Dr. Shiv K. Sarin (India)
Dr. Jose Sollano (Philippines)
Dr. Tawesak Tanwandee (Thailand)
Dr. Arndt Vogel (Canada)
Dr. Lai Wei (China)
Dr. Carmen C. L. Wong (Hong Kong)
Dr. Changhoon Yoo (Korea)

In alphabetical order

Invited Guests/Speakers/Chairs/ Scientific Committee from Japan

Dr. Norio Akuta
Dr. Yasuhiro Asahina
Dr. Masanori Atsukawa
Dr. Makoto Chuma
Dr. Hirotoshi Ebinuma
Dr. Hirayuki Enomoto
Dr. Naoto Fujiwara
Dr. Takumi Fukumoto
Dr. Junji Furuse
Dr. Takuya Genda
Dr. Kenichi Harada
Dr. Kiyoshi Hasegawa
Dr. Etsuro Hatano
Dr. Yoichi Hiasa
Dr. Hayato Hikita
Dr. Naoki Hiramatsu
Dr. Atsushi Hiraoka
Dr. Yosuke Hirotsu
Dr. Yuji Iimuro
Dr. Masafumi Ikeda
Dr. Tadashi Ikegami
Dr. Kenichi Ikejima
Dr. Toru Ishikawa
Dr. Kiyoaki Ito
Dr. Shinji Itoh
Dr. Yoshito Itoh
Dr. Tatehiro Kagawa
Dr. Masaki Kaibori
Dr. Keisuke Kakisaka
Dr. Tatsuo Kanda
Dr. Tatsuya Kanto
Dr. Naoya Kato
Dr. Norifumi Kawada
Dr. Takumi Kawaguchi
Dr. Tomokazu Kawaoka
Dr. Takahiro Kodama
Dr. Shohei Komatsu
Dr. Mina Komuta
Dr. Yasuteru Kondo
Dr. Masatoshi Kudo
Dr. Masayuki Kurosaki
Dr. Teiji Kuzuya
Dr. Tsutomu Masaki
Dr. Satoshi Mochida
Dr. Hitoshi Mochizuki
Dr. Manabu Morimoto
Dr. Naoki Morimoto
Dr. Mitsuhiko Moriyama
Dr. Takamichi Murakami
Dr. Kazumoto Murata
Dr. Hidenari Nagai
Dr. Hiroaki Nagano
Dr. Hayato Nakagawa
Dr. Atsushi Nakajima
Dr. Nobuhiro Nakamoto
Dr. Yasunari Nakamoto
Dr. Kazuhiko Nakao
Dr. Naoshi Nishida
Dr. Kazuhiro Nouso
Dr. Shuntaro Obi
Dr. Sadahisa Ogasawara
Dr. Kazuyoshi Ohkawa
Dr. Hiroshi Ohno
Dr. Hironao Okubo
Dr. Takuji Okusaka
Dr. Masao Omata
Dr. Masayuki Otsuka
Dr. Motoyuki Otsuka
Dr. Issei Saeki
Dr. Michiie Sakamoto
Dr. Naoya Sakamoto
Dr. Tatsuhiro Shibata
Dr. Shuichiro Shiina
Dr. Mitsuo Shimada
Dr. Masahito Shimizu
Dr. Junichi Shindoh
Dr. Ken Shirabe
Dr. Toshifumi Tada

Dr. Koichi Takaguchi
Dr. Taro Takami
Dr. Tetsuo Takehara
Dr. Akinobu Taketomi
Dr. Nobuharu Tamaki
Dr. Shinji Tanaka
Dr. Yasuhito Tanaka
Dr. Toshihiro Tanaka
Dr. Ryosuke Tateishi
Dr. Shuji Terai
Dr. Takeshi Terashima
Dr. Yosuke Togashi
Dr. Hidenori Toyoda
Dr. Kaoru Tsuchiya
Dr. Makoto Ueno
Dr. Yoshiyuki Ueno
Dr. Michiaki Unno
Dr. Masaru Wakatsuki
Dr. Takahiro Yamasaki
Dr. Taro Yamashita
Dr. Tatsuya Yamashita
Dr. Hirohisa Yano
Dr. Hiroshi Yatsuhashi
Dr. Osamu Yokosuka
Dr. Hiroshi Yoshida
Dr. Hitoshi Yoshiji
Dr. Tomoharu Yoshizumi

In alphabetical order

Organizing Committee

Local Organizing Committee

President: Dr. Naoya Kato

Honorary President: Dr. Masao Omata

Vice-President: Dr. Junji Furuse, Dr. Masatoshi Kudo

Scientific Committee:	Dr. Michiie Sakamoto	Dr. Masayuki Kurosaki	Dr. Tatsuya Kanto
	Dr. Tsutomu Masaki	Dr. Naoya Sakamoto	Dr. Kiyoshi Hasegawa
	Dr. Ryosuke Tateishi	Dr. Masafumi Ikeda	
Treasurer:	Dr. Osamu Yokosuka	Dr. Shuichiro Shiina	Dr. Masayuki Otsuka
	Dr. Shuntaro Obi		
Secretary General:	Dr. Sadahisa Ogasawara		

APASL Steering Committee

Chairman of Steering Committee:	Dr. Shiv K. Sarin (India)
President:	Dr. Lai Wei (China)
Immediate Past President:	Dr. Shuichiro Shiina (Japan)
President Elect:	Dr. Necati Ormeci (Turkey)
Secretary General-cum-Treasurer:	Dr. Manoj K. Sharma (India)

Past Presidents:

Dr. Laurentius A. Lesmana (Indonesia)	Dr. A. Kadir Dokmeci (Turkey)
Dr. Jose Sollano (Philippines)	Dr. Osamu Yokosuka (Japan)
Dr. Masao Omata (Japan)	Dr. Jinlin Hou (China)
Dr. Dong Jin Suh (Korea)	Dr. Barjesh Chander Sharma (India)
Dr. George K. K. Lau (China)	Dr. Diana A. Payawal (Philippines)
Dr. Ji Dong Jia (China)	Dr. Rino Gani (Indonesia)
Dr. Teerha Piratvisuth (Thailand)	Dr. Tawesak Tanwandee (Thailand)
Dr. Jia-Horng Kao (Taiwan)	Dr. Jin Mo Yang (Korea)
Dr. Darrell Crawford (Australia)	Dr. Han-Chieh Lin (Taiwan)

APASL Executive Council

President: Dr. Lai Wei (China)
Immediate Past President: Dr. Shuichiro Shiina (Japan)
President Elect: Dr. Necati Ormeci (Turkey)
Secretary General-cum-Treasurer: Dr. Manoj K. Sharma (India)
Executive Council Members:

Dr. Sang Hoon Ahn (Korea)
Dr. Gulnara Aghayeva (Azerbaijan)
Dr. Chun-Jen Liu (Taiwan)
Dr. Mamun-Al-Mahtab (Bangladesh)
Dr. Rakhi Maiwall (India)
Dr. Elizabeth Powell (Australia)
Dr. Yoshiyuki Ueno (Japan)
Dr. Jian Zhou (China)

Conference Information

Registration Fee and Category

Term / Category	Early Bird until July 31, 2024	Pre-Registration September 20, 2024	On Site
APASL Member	JPY 20,000	JPY 25,000	JPY 30,000
Non-Member	JPY 30,000	JPY 35,000	JPY 40,000
Accepted Abstract Submitter	JPY 25,000	JPY 30,000	JPY 35,000
Trainee / Resident	JPY 15,000	JPY 20,000	JPY 25,000
Medical Student	JPY 3,000	JPY 5,000	JPY 10,000
Accompanying Person	JPY 5,000	JPY 5,000	JPY 5,000

JPY=Japanese Yen
*APASL Members who have paid 2024 Membership Fee can apply for discounted registration fee.

Onsite Registration/PC Pre-view Hours

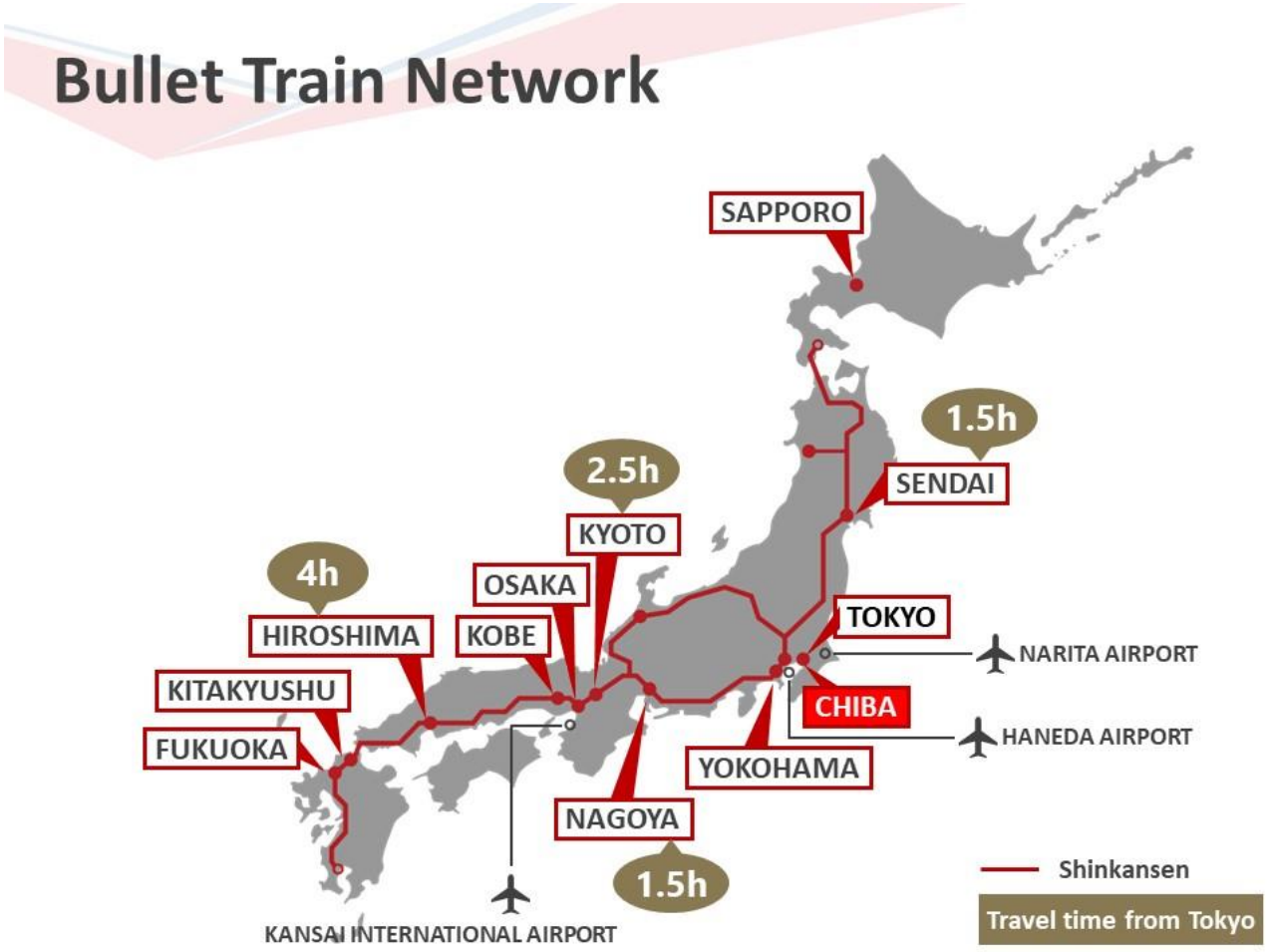
September 24 (Tuesday) 8:00-18:00 (JST)
September 25 (Wednesday) 7:00-17:00 (JST)

Memo

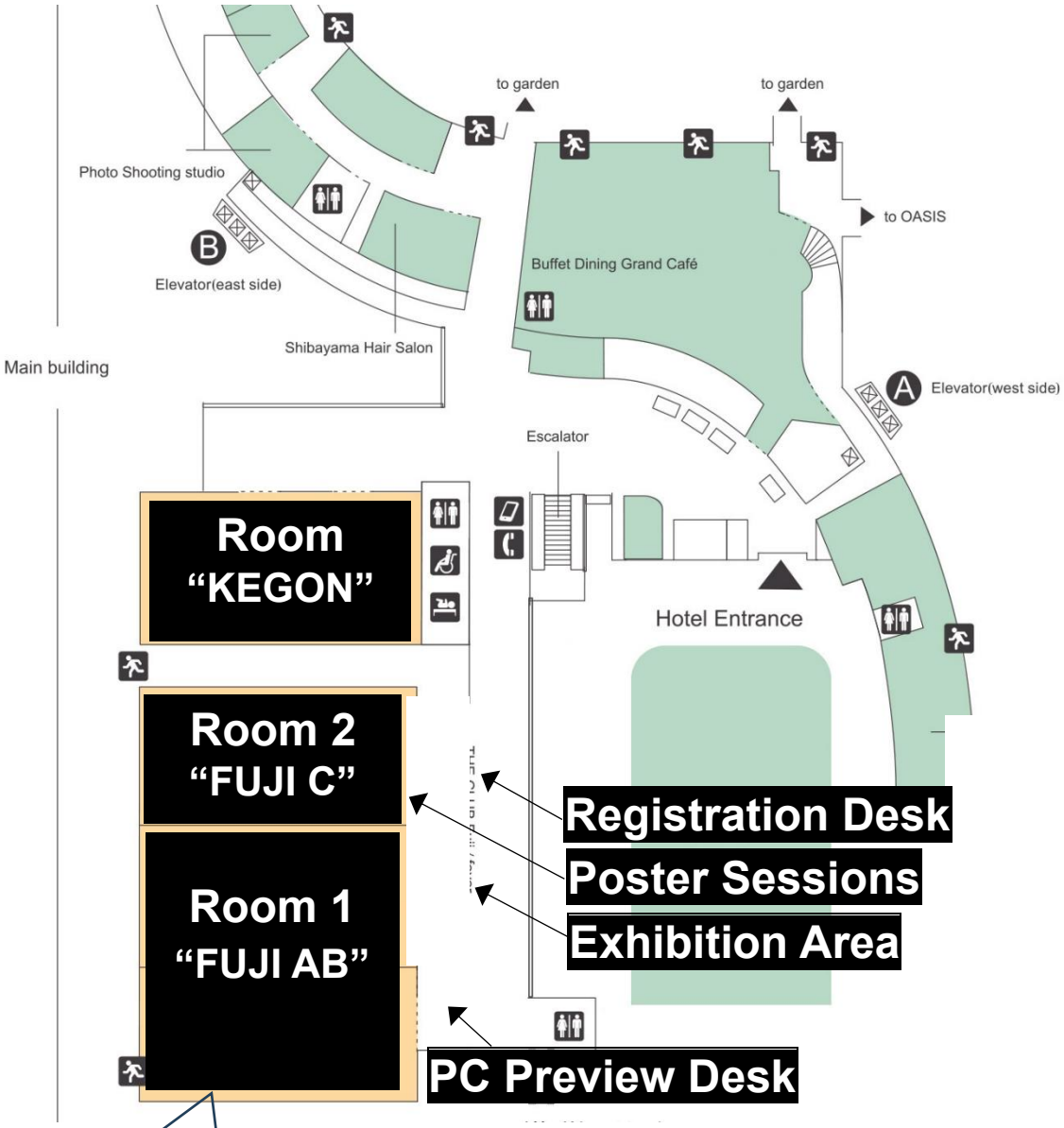
Venue

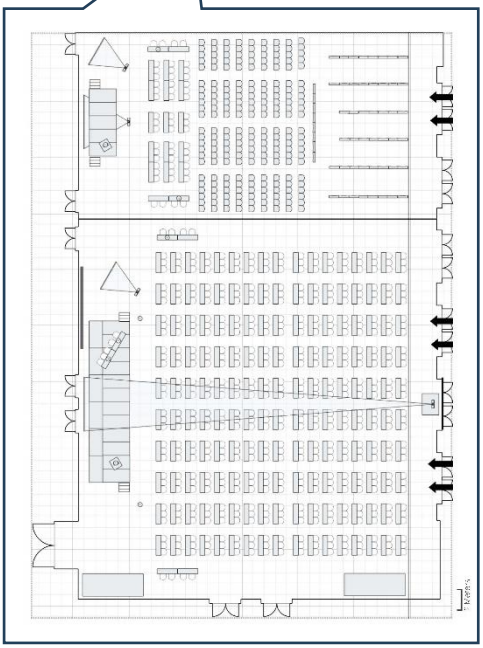
Sheraton Grande Tokyo Bay Hotel

Address:	1-9 Maihama Urayasu, Japan 279-0031
Tel:	+81-(0)47-355-5555
Location:	[From Narita Airport] Approx. 1 hour 20 minutes by Limousine Bus to the venue. [From Haneda Airport] Approx. 1 hour 10 minutes by Limousine Bus to the venue. [From Tokyo Station] Approx. 25 minutes by a train to the venue.
URL:	https://www.marriott.com/en-us/hotels/tyosi-sheraton-grande-tokyo-bay-hotel/overview/



Floor Plan: 1F, Sheraton Grande Tokyo Bay Hotel





Room 1: "The Club Fuji AB" 1st Floor
Room 2: "The Club Fuji C", 1st Floor
Welcome Reception: "Kegon", 1st Floor
Cloak: Foyer, 1st Floor
Registration: Foyer, 1st Floor
PC Preview Desk: Foyer, 1st Floor
Poster Sessions: Room 2 "The Club Fuji C"
Speakers/Chairs Ready Room:
"VIP A", "VIP B", 1st Floor,
"Akemi A", "Akemi B", 2nd Floor
Faculty Lounge: "Irifune A", 2nd Floor
Secretariat Room: "Irifune B", 2nd Floor

Instruction for Oral Presentation

- Please complete your registration of presentation data at the Data Pre-View Desk until 30 min. before your presentation time.
- The open hours of Data Pre-View Desk are as follows.

  September 24 (Tuesday) 8:00-18:00 (JST)

  September 25 (Wednesday) 7:00-17:00 (JST)

- Please be seated at the “next speaker’s seat” at least 10 minutes before your presentation. The seat will be located forward near the podium.
- The slides which you have submitted in advance for the presentation are prepared on the computer of the podium.
- After presentation, the discussion time (a question-and-answer session) will be held according to the moderator’s instructions.
- The PC which will be set at the podium is OS: Windows 10 (PowerPoint: 2013, 2021) with DVD Super Multi Drive function.
- Please bring your data by USB memory stick, CDR, or DVDR (Disk at Once).
- To avoid garbled characters, please use standard font which is originally installed by OS.
- Please put your name on your data file.
- If you bring your movies by data file, please prepare the file which can be played by standard Windows Media Player.
- Backup data by another media should be kept by presenter.
- The projector’s screen resolution is set at 16:9 FULL HD. Please make your PPT data the necessary preparation if needed (4:3 XGA is also projectable with a size smaller, black flamed on both left and right sides).
- Please operate your PPT data by yourself at the podium.

<If you bring your own PC>

- Please make sure that your PC has HDMI terminal for monitor output. (Some compact PC needs another connector. In case of that, please carry your own connector.)
- Macintosh and Key Note are acceptable only if you will bring your own PC (Please carry your own connector).
- Please bring battery adapter to avoid battery off. Because sometimes screen saver or power saving system could be a reason of battery off, please set your PC appropriately.

<Disclosure of COI>

Regarding the disclosure of conflicts of interest on the second slide, please include one of the slides such as follows.

Instruction for Chairs

Please be seated at the “next chair’s seat” at least 10 minutes before the session starts. The seat will be located forward near the stage.

After presentation, the discussion time (a question-and-answer session) will be held according to the moderator’s instructions. The participants will ask questions using the microphone at the conference hall.

Instruction for Poster Presentation

- A panel width 90cm×length 210cm will be provided for each poster as following sample.
- Poster number will be prepared by secretariat.
- Title and author’s name are required to be prepared by each presenter.
- Pins for display will be provided at each poster panel.
- Location: Poster Session will be performed at Room 2 “The Club Fuji C”.
- Presentation Time: 5min. Presentation + 3min. Discussion = Total 8min. for each poster.
- For those who have not removed posters until removal time, please accept that the secretariat will discard any posters that have remained.
- Regarding the disclosure of conflicts of interest, please include one of the conflicts of interest disclosure slides using template.

* Poster Presentation is scheduled as follows.

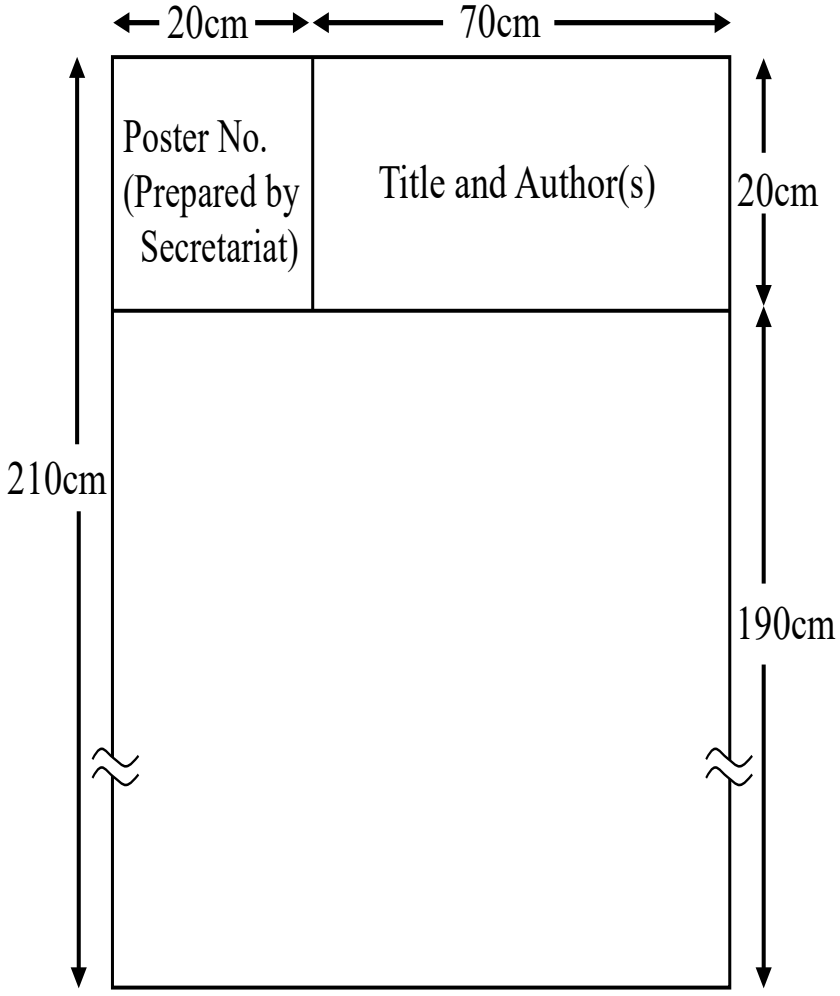
For Presenter on Day 1 September 24 (Tuesday)

Poster Attachment: 8:00-10:00 on September 24 (Tuesday)
Poster Session: 17:50-18:50 on September 24 (Tuesday)
Awarding Ceremony: 19:00-19:20 on September 24 (Tuesday) at Room “Kegon”
Poster Removal: 18:50-21:00 on September 24 (Tuesday)

For Presenter on Day 2 September 25 (Wednesday)

Poster Attachment: 8:00-10:00 on September 25 (Wednesday)
Poster Session: 16:20-17:20 on September 25 (Wednesday)
Awarding Ceremony: 17:30-17:50 on September 25 (Wednesday) at Room 1 “The Club Fuji AB”
Poster Removal: 17:20-18:30 on September 25 (Wednesday)

Poster Panel



Awards

Excellent papers will be awarded as “Presidential Award”, “Investigator Award”, “Travel Award”.
The Awardees will be presented at the Awarding Ceremony, for Day 1’s presenters at 19:00-19:20 on September 24, and for Day 2’s presenters at 17:30-17:50 on September 25.
All the attendees are requested to join voting on site for selecting excellent abstracts.
As a thanks for participation in the vote, a small lottery will be held at the Awarding Ceremony.
You may be able to win a prize (including free ticket to the nearby world-famous amusement park)!

Presidential Award

“APASL Oncology 2024 Chiba Presidential Award” will be awarded to whom performed the most excellent presentation in APASL Oncology 2024 Chiba to encourage to their research and progress.

Investigator Award

The purpose of the “APASL Oncology 2024 Chiba Investigator Award” is to praise outstanding examples of excellence amongst those involved in research training in the early stages of their career.

Travel Award

“APASL Oncology 2024 Chiba Travel Award” will be awarded to whom performed the excellent presentation traveling to the onsite venue in APASL Oncology 2024 Chiba.

Contact

APASL Oncology 2024 Chiba Scientific Secretariat

Department of Gastroenterology, Chiba University, Japan

APASL Oncology 2024 Chiba Congress Secretariat

c/o Academia Support Japan
Email: info@apasl-oncology2024.org
Tel: +81-3-6380-0102 Fax: +81-3-6380-0103

APASL Central Office (APASL Secretariat-Tokyo)

Asian Pacific Association for the Study of the Liver [APASL]
1-24-7-920, Shinjuku, Shinjuku-ku, Tokyo, 160-0022 Japan
Email: apasl_secretariat@apasl.info
Tel: +81-3-5312-7686 Fax: +81-3-5312-7687

Sponsors and Support Organizations

The Organizing Committee of the APASL Oncology 2024 Chiba would like to express sincere gratitude to the following sponsors and organizations for supporting this conference.

Diamond Sponsors

AbbVie G.K.

AstraZeneca

Chugai Pharmaceutical Co., Ltd.

Gilead Sciences K.K.

Platinum Sponsor

Eisai Co., Ltd.

Gold Sponsors

FUJIFILM Wako Pure Chemical Corporation
Incyte Biosciences Japan G.K.
Miyarisan Pharmaceutical Co., Ltd.

Silver Sponsors

Bristol-Myers Squibb K.K.
Medical Scanning
MSD K.K.
Nippon Kayaku Co., Ltd.
Takeda Pharmaceutical Company Limited

Bronze Sponsors

ASKA Pharmaceutical Co., Ltd.
Astellas Pharma Inc.
Biotech Lab Inc.
Eli Lilly and Company
Kowa Company Ltd.
Nacalai Tesque, Inc.
Nobelpharma Co., Ltd.
Novo Nordisk Pharma Ltd.
Olympus Marketing, Inc.
Viatris Inc.

Support Organizations

Japan Liver Cancer Association
The Japan Society of Hepatology
Chiba Convention Bureau and International Center

APASL Oncology 2024 Program at a Glance Day 1

	September 24 (Tuesday) 2024			
	Room 1	**Room 2**	**Room2**	**Foyer**
08:00	8:00- Registration			
	8:30-8:40 **Opening Ceremony**			
09:00	8:40-10:20 **Session 1: Current Insights into Molecular Pathways and Mechanisms in Liver Cancer Development**			
10:00			**Poster Viewing**	**Exhibition**
	10:30-11:10 **Special Lecture 1: Hepatitis Treatment: A Long-Term Investment in Liver Cancer Prevention and Survival**			
11:00				
	11:20-12:20 **Session 2: APASL HCC Guideline and the Endeavor of A-HOC**			
12:00				
13:00	12:30-13:30 **Luncheon Seminar 1** (Gilead Sciences K.K.)	12:30-13:30 **Luncheon Seminar 2** (Chugai Pharmaceutical Co., Ltd.)		
14:00	13:40-15:20 **Session 3: Advances in Systemic Treatment Options for Liver Cancer**			
15:00				
16:00	15:30-16:30 **Sponsored Seminar 1** (Eisai Co., Ltd.)	15:30-16:30 **Sponsored Seminar 2** (AbbVie G.K.)		
17:00	16:40-17:40 **Plenary Session** <Voting for awards by all attendees>			
18:00		17:50-18:50 **Poster Session Day 1** <Voting for awards by all attendees>		
19:00	19:00-19:20 **Awarding Ceremony Day 1*** 19:20-20:30 **Welcome Reception***			

*Awarding Ceremony Day 1 and Welcome Reception will be held in the Room “KEGON”.

APASL Oncology 2024 Program at a Glance Day 2

	September 25 (Wednesday) 2024			
	Room 1	**Room 2**	**Room 2**	**Foyer**
	7:00- Registration			
8:00	7:30-8:30 **Morning Seminar 1** (Incyte Biosciences Japan G.K.)	7:30-8:30 **Morning Seminar 2** (Miyarisan Pharmaceutical Co. Ltd.)		
9:00	8:40-9:40 **Session 4: From Mechanisms to Treatment: Targeting the Tumor Microenvironment and Immune Landscape**		**Poster Viewing**	**Exhibition**
10:00	9:50-10:50 **Sponsored Seminar 3** (Chugai Pharmaceutical Co., Ltd.)	9:50-10:50 **Sponsored Seminar 4** (Gilead Sciences K.K.)		
11:00	11:00-11:40 **Special Lecture 2: Hepatology in Asia: Navigating the Landscape of Liver Diseases**			
12:00	11:50-12:50 **Luncheon Seminar 3** (AbbVie G.K.)	11:50-12:50 **Luncheon Seminar 4** (Eisai Co., Ltd.)		
13:00	13:00-15:00 **Session 5: Integrated Therapeutic Strategies for Liver Cancer: A Multidisciplinary Perspective**			
14:00				
15:00				
16:00	15:10-16:10 **Sponsored Seminar 5** (FUJIFILM Wako Pure Chemical Corporation)			
17:00		16:20-17:20 **Poster Session Day 2** <Voting for awards by all attendees>		
18:00	17:30-17:50 **Awarding Ceremony Day 2** 17:50-17:55 **Closing Ceremony**			

Memo

APASL Oncology 2024 Chiba

"Genomics Meets Immunology:

Interdisciplinary Approach for Liver Cancer"

Scientific Program

APASL Oncology 2024 Chiba Scientific Program

Day 1: September 24 (Tuesday) 2024

Room 1 (The Club Fuji AB)

8:30-8:40 Opening Ceremony

Opening Remarks: Dr. Naoya Kato, President of APASL Oncology 2024 Chiba

8:40-10:20 Session 1: Current Insights into Molecular Pathways and Mechanisms in Liver Cancer Development

Moderators: Dr. Lai Wei (China), Dr. Motoyuki Otsuka (Japan), Dr. Taro Yamashita (Japan)
Commentators: Dr. Yujin Hoshida (USA), Dr. Takahiro Kodama (Japan)

S1-1 Deciphering Liver Cancer: Molecular Pathways, Mechanisms, and Identifying High-Risk Groups for Carcinogenesis and Recurrence
Dr. Yujin Hoshida (USA)

S1-2 Leveraging Genomic Insights to Advance Liver Cancer Diagnosis and Treatment
Dr. Tatsuhiro Shibata (Japan)

S1-3 Liver Metabolism as a Driver of Hepatocarcinogenesis: Emerging Concepts and Future Directions
Dr. Hayato Nakagawa (Japan)

S1-4 Unraveling the Complexity of Tumor Heterogeneity in Hepatocellular Carcinoma: Intra-tumoral and Inter-tumoral Perspectives
Dr. Yosuke Hirotsu (Japan)

S1-5 Carcinogenesis and Its Evolution of Primary Liver Cancers from a Pathological Perspective
Dr. Mina Komuta (Japan)

10:30-11:10 Special Lecture 1: Hepatitis Treatment: A Long-Term Investment in Liver Cancer Prevention and Survival

Moderators: Dr. Diana A. Payawal (Philippines), Dr. Norifumi Kawada (Japan)

SL1-1 Prevention of Primary Liver Cancer, China Perspective
Dr. Lai Wei (China)

SL1-2 Management of Portal Hypertension and its Complications in HCC: A 2024 Update
Dr. Shiv K. Sarin (India)

11:20-12:20 Session 2: APASL HCC Guideline and the Endeavor of A-HOC

Moderators: Dr. Shiv K. Sarin (India) , Dr. Masao Omata (Japan)
Commentators: Dr. Oidov Baatarkhuu (Mongolia), Dr. Lai Wei (China)

S2-1 Landscape of Western HCC Guidelines
Dr. Arndt Vogel (Canada)

S2-2 The Latest APASL Clinical Practice Guideline on Systemic Therapy for Hepatocellular Carcinoma
Dr. George K. K. Lau (China)

S2-3 A-HOC Start-up and Current State
Dr. Hitoshi Mochizuki (Japan)

12:30-13:30 Luncheon Seminar 1 (Gilead Sciences K.K.)

Moderator: Dr. Naoki Morimoto (Japan)

"Current Topics on Viral Hepatitis"

LS1-1 Hepatitis C Treatment Progress Towards Elimination and Post-SVR Issues
Dr. Toshifumi Tada (Japan)

LS1-2 Innovative Strategies for Treating HBV-Related HCC: Insights from Basic Research
Dr. Motoyuki Otsuka (Japan)

13:40-15:20 Session 3: Advances in Systemic Treatment Options for Liver Cancer

Moderators: Dr. Rino Gani (Indonesia), Dr. Masafumi Ikeda (Japan), Dr. Masayuki Kurosaki (Japan)
Commentators: Dr. George K. K. Lau (China), Dr. Arndt Vogel (Canada)

S3-1 Current Systemic Therapy in Liver Cancer: Present Achievements and Future Directions
Dr. Arndt Vogel (Canada)

S3-2 Advancing Systemic Therapy for Liver Cancer: Clinical Practice Insights and Research Initiatives to Meet Unmet Needs
Dr. Changhoon Yoo (Korea)

S3-3 Harnessing the Power of Real-World Data to Address Clinical Challenges in Systemic Therapy for Advanced Hepatocellular Carcinoma
Dr. Sadahisa Ogasawara (Japan)

S3-4 Pushing the Boundaries of Liver Cancer Treatment: Synergizing Locoregional Therapy and Immunotherapy
Dr. Masatoshi Kudo (Japan)

S3-5 Personalized Approaches to Liver Cancer Management: Molecular and Immunological Landscape to Develop Novel Strategies
Dr. Shinji Tanaka (Japan)

15:30-16:30 Sponsored Seminar 1 (Eisai Co., Ltd.)

Moderator: Dr. Ryosuke Tateishi (Japan)

SS1 Pushing the Envelope for Surgical Management of Advanced Hepatocellular Carcinoma
Dr. Junichi Shindoh (Japan)

16:40-17:40 Plenary Session

Moderators: Dr. Jose Sollano (Philippines), Dr. Tatsuya Yamashita (Japan)
Commentators: Dr. Hayato Hikita (Japan), Dr. Kaoru Tsuchiya (Japan)

O-1 10041
Long-term Hepatocellular Carcinoma Occurrence Rate after Administration of Nucleos(t)ide Analogues in Patients with Persistent HBV Infection
Dr. Kazuhiro Murai (Japan)

O-2 10016
Spatial Omics Analysis of the Proximity of PD-L1(+) Tumor-Associated Macrophage and CD8T cell Interaction Promoting Hepatocellular Carcinoma Progression
Dr. Takuto Nosaka (Japan)

O-3 10064
Comparative Pathological and Comprehensive Genomic Analysis for Differential Diagnosis between IM and MC
Dr. Kenji Amemiya (Japan)

O-4 10118

Relationship between Anti-tumor Response and Immune-mediated Adverse Events Requiring High-dose Corticosteroids in Unresectable Hepatocellular Carcinoma Treated with Durvalumab plus Tremelimumab

Dr. Takanori Ito (Japan)

O-5 10154

Prognostic Factors after Carbon-ion Rradiotherapy: A Study Based on Multi-institutional Registry Data

Dr. Kei Shibuya (Japan)

O-6 10163

Contour Prognostic Model: Effect of Diameter and Number of Hepatocellular Carcinomas on Survival after Resection, Trans-Arterial Chemoembolization, and Ablation (The Liver Cancer Study Group of Japan)

Dr. Yoshikuni Kawaguchi (Japan)

17:50-18:50 Poster Session Day 1

At Room 2 “The Club Fuji C” , 1st Floor, Sheraton Grande Tokyo Bay Hotel

19:00-19:20 Awarding Ceremony Day 1

At Room “Kegon”, 1st Floor, Sheraton Grande Tokyo Bay Hotel

19:20-20:30 Welcome Reception

At Room “Kegon”, 1st Floor, Sheraton Grande Tokyo Bay Hotel

Day 1: September 24 (Tuesday) 2024

Room 2 (The Club Fuji C)

12:30-13:30 Luncheon Seminar 2 (Chugai Pharmaceutical Co., Ltd.)

Moderator: Dr. Masayuki Kurosaki (Japan)

LS2-1 Remaining Clinical Questions and Unmet Needs in the Era of Immunotherapy for Unresectable Hepatocellular Carcinoma
Dr. Takeshi Terashima (Japan)

LS2-2 Future Perspectives of Systemic Chemotherapy and Surgery in the Treatment of Hepatocellular Carcinoma
Dr. Shohei Komatsu (Japan)

15:30-16:30 Sponsored Seminar 2 (AbbVie G.K.)

Moderator: Dr. Tadashi Ikegami (Japan)

SS2 DAA Treatment for Chronic Hepatitis C and Future Challenges
Dr. Nobuharu Tamaki (Japan)

17:50-18:50 Poster Session Day 1

Day 2: September 25 (Wednesday) 2024

Room 1 (The Club Fuji AB)

7:30-8:30 Morning Seminar 1 (Incyte Biosciences Japan G.K.)

Moderator: Dr. Masayuki Otsuka (Japan)

MS1 New Treatment Strategy for Intrahepatic Cholangiocarcinoma
Dr. Makoto Ueno (Japan)

8:40-9:40 Session 4: From Mechanisms to Treatment: Targeting the Tumor Microenvironment and Immune Landscape

Moderators: Dr. Tatsuya Kanto (Japan), Dr. Yasuhito Tanaka (Japan)
Commentator: Dr. Carmen C. L. Wong (China)

S4-1 Tumor Microenvironment and Immune Response in Cancer
Dr. Yosuke Togashi (Japan)

S4-2 Advancements and Future Directions in the Study of the Immune Landscape of Liver Cancer
Dr. Carmen C. L. Wong (China)

S4-3 Challenging in Biomarker Discovery: Targeting the Tumor Microenvironment in Hepatocellular Carcinoma
Dr. Takahiro Kodama (Japan)

9:50-10:50 Sponsored Seminar 3 (Chugai Pharmaceutical Co., Ltd.)

Moderator: Dr. Masafumi Ikeda (Japan)

SS3 Real-World Clinical Impact of Atezolizumab plus Bevacizumab in Patients with Advanced Hepatocellular Carcinoma - A 4-Year Experience
Dr. Teiji Kuzuya (Japan)

11:00-11:40 Special Lecture 2: Hepatology in Asia: Navigating the Landscape of Liver Diseases

Moderators: Dr. A. Kadir Dokmeci (Turkey), Dr. Osamu Yokosuka (Japan)

SL2-1 HCC Etiology, Incidence, Diagnosis, Management and Survival in Mongolia, Update of A-HOC Studies
Dr. Jazag Amarsanaa (Mongolia)

SL2-2 Hepatology in Asia: Navigating the Landscape of Liver Diseases (HCC)
Dr. Masao Omata (Japan)

11:50-12:50 Luncheon Seminar 3 (AbbVie G.K.)

Moderator: Dr. Yoshiyuki Ueno (Japan)

"Topics on Treatment of Liver Diseases, HCV Infection and HCC"

LS3-1 Multidisciplinary Treatment Including Ultra-FP, iCIs and Ablation Therapy should be Considered to Control HCC
Dr. Yasuteru Kondo (Japan)

LS3-2 Pharmacokinetics of Direct-Acting Antiviral Therapy for Hepatitis C Virus Infection
Dr. Hironao Okubo (Japan)

13:00-15:00 Session 5: Integrated Therapeutic Strategies for Liver Cancer: A Multidisciplinary Perspective

Moderators: Dr. Tawesak Tanwandee (Thailand), Dr. Kiyoshi Hasegawa (Japan), Dr. Shuntaro Obi (Japan), Dr. Naoya Sakamoto (Japan)
Commentators: Dr. Stephen Lam Chan (China), Dr. Yi-Hsiang Huang (Taiwan)

S5-1 From Early to Advanced Stages: Navigating Hepatocellular Carcinoma Treatment with Systemic Therapy
Dr. Stephen Lam Chan (China)

S5-2 Multifaceted Strategies for Hepatocellular Carcinoma in Asia: Improving Patient Outcomes with Optimal Treatment Modalities
Dr. Yi-Hsiang Huang (Taiwan)

S5-3 Surgical Resections in Hepatocellular Carcinoma: Evolving in Tandem with Advancements in Systemic Therapy
Dr. Shinji Itoh (Japan)

S5-4 The Role of Percutaneous Ablation in the Treatment of Liver Cancer: A Response to Shifting Disease Patterns and Treatment Landscapes
Dr. Ryosuke Tateishi (Japan)

S5-5 The Evolving Landscape of Transarterial Therapy for Liver Cancer: Current Practices and Emerging Trends
Dr. Toshihiro Tanaka (Japan)

S5-6 Radiation Therapy in Liver Cancer: Insights into Current Impact and Future Prospects
Dr. Masaru Wakatsuki (Japan)

15:10-16:10 Sponsored Seminar 5 (FUJIFILM Wako Pure Chemical Corporation)

Moderator: Dr. Masao Omata (Japan)

SS5 AFP-L3: An Old and New Marker Specific for the Management of HCC

Dr. Hidenori Toyoda (Japan)

16:20-17:20 Poster Session Day 2

At Room 2 “The Club Fuji C” , 1st Floor, Sheraton Grande Tokyo Bay Hotel

17:30-17:50 Awarding Ceremony Day 2

17:50-17:55 Closing Ceremony

Closing Remarks: Dr. Naoya Kato, President of APASL Oncology 2024 Chiba

Day 2: September 25 (Wednesday) 2024

Room 2 (The Club Fuji C)

7:30-8:30 Morning Seminar 2 (Miyarisan Pharmaceutical Co., Ltd.)

Moderator: Dr. Hitoshi Yoshiji (Japan)

MS2 Gut Microbiota in Host Health and Diseases Including Gastrointestinal Cancers

Dr. Hiroshi Ohno (Japan)

9:50-10:50 Sponsored Seminar 4 (Gilead Sciences K.K.)

Moderator: Dr. Kazumoto Murata (Japan)

SS4 Prediction and Prevention of Hepatocellular Carcinoma in Chronic Liver Diseases

Dr. Taro Yamashita (Japan)

11:50-12:50 Luncheon Seminar 4 (Eisai Co., Ltd.)

Moderator: Dr. Masatoshi Kudo (Japan)

"Treatment Strategy for Hepatocellular Carcinoma Focused on Tumor Microenvironment"

LS4-1 Hepatocellular Carcinoma Treatment in the Era of Combined Immunotherapy -Future Role of Lenvatinib in Light of the Tumor Immune Microenvironment-

Dr. Naoto Fujiwara (Japan)

LS4-2 Lenvatinib-based Treatment Strategy for Unresectable Hepatocellular Carcinoma

Dr. Issei Saeki (Japan)

16:20-17:20 Poster Session Day 2

Poster Sessions

Day 1: September 24 (Tuesday) 2024

Room 2 (The Club Fuji C) 17:50-18:50

Poster Session 1: Systemic Therapy [Early Carrer] (1)

Chair: Dr. Naoki Morimoto (Japan)

P-01 10019
An Effective Prognostic Risk Model Related to Fatty Acid Metabolism in Hepatocellular Carcinoma
Dr. Xiaobin Li (China)

P-02 10042
Potential Correlation between Changes in Serum FGF21 Levels and Lenvatinib-Induced Appetite Loss in Patients with Unresectable Hepatocellular Carcinoma
Dr. Risako Kohya (Japan)

P-03 10065
The Importance of Assessing Energy Malnutrition in Atezolizumab/Bevacizumab Therapy
Dr. Maho Egusa (Japan)

P-04 10114
Understanding the Disease Stage of Intermediate Stage Hepatocellular Carcinoma (HCC) - Analysis of Initial Treatment and Tumor Conditions
Dr. Teppei Akatsuka (Japan)

P-05 10117
Analysis of Immune-mediated Adverse Event Colitis Induced by Combination Therapy with Durvalumab and Tremelimumab for Advanced Hepatocellular Carcinoma
Dr. Makoto Fujiya (Japan)

P-06 10126
Pathophysiology of Immune Related Liver Injury from a Clinicopathological Perspective
Dr. Ryo Izai (Japan)

P-07 10150
Sorafenib Induced Stevens-Johnson Syndrome after Immune Checkpoint Inhibitor Treatment in a Patient of Hepatocellular Carcinoma
Dr. Kosuke Kojima (Japan)

Poster Session 2: Basic Research [Early Career]

Chair: Dr. Yasunari Nakamoto(Japan)

P-08 10012
Solanum Torvum Induces Ferroptosis to Suppress Hepatocellular Carcinoma through Suppression of GPX4 and Activation of HO-1
Dr. Hsiang-Chun Lai (Taiwan)

P-09 10018
Chai Qi Yi Gan Granule Restores Gut Microbial Balance and Modulates Lipid Metabolism to Suppress Hepatocellular Carcinoma
Dr. Xiaobin Li (China)

P-10 10066
Integrated Single-Cell and Bulk RNA Sequencing Reveals CCR2-High Neutrophils in Gr1+ Myeloid Lineages of CRLM Mice
Dr. Zijun Yan (China)

P-11 10133
Early Width of Dispersion of Monocytes Complexity (MO-WX) as a Discriminating Tool of Hepatocellular Carcinoma in Liver Cirrhotic: A Pilot Study of Novel Marker with Leukocytes Cell Population Data
Dr. Dwijo A. Sindhughosa (Indonesia)

P-12 10153
Biflavonoid Derivatives as Potential CDK1 Inhibitors in Hepatocellular Carcinoma: Investigation via Virtual Screening and Molecular Interaction Analysis
Dr. Reny Rosalina (Indonesia)

P-13 10125
Withdrawn

P-14 10049
Dietary Elaidic Acids Promotes Malignant Behavior of HepG2 Cells via NF-kappaB Signaling Pathway
Dr. Xiao Hu (China)

Poster Session 3: Liver Cirrhoss and Portal Hypertension [Early Career]

Chair: Dr. Masanori Atsukawa (Japan)

P-15 10015
Association between Osteosarcopenia and Prognosis in Liver Cirrhosis Complicated with Portal Hypertension
Dr. Arisa Saito (Japan)

P-16 10017
Reasons for Liver Regeneration Failure, How to Save it?
Dr. Bowen Liu (China)

P-17 10050
Long-term L-carnitine Supplementation Suppresses Skeletal Muscle Mass Loss by Decreasing the Expression of Interleukin-6 in Patients with Hepatocellular Carcinoma
Dr. Yu Takeda (Japan)

P-18 10052
Effect of MAFLD Criteria on Postoperative Recurrence of NBNC-HCC
Dr. Yusuke Johira (Japan)

P-19 10092
Effectiveness of Multidisciplinary Inpatient Treatment with Personalized Diet and Exercise Therapy for Steatotic Liver Disease
Dr. Eriksson Yasuka (Japan)

P-20 10156
Virtual Screening of Resveratrol-derived Compounds for Targeting the TGF-β 1 Receptor in Liver Fibrosis
Dr. Rian Ka Praja (Indonesia)

P-21 10144
Mathematical Modelling for Investigating the Inconsistencies between Transient Elastography and Liver Biopsy Results in Assessing Liver Fibrosis in Patients with Chronic Viral Hepatitis
Dr. Prihantini Prihantini (Indonesia)

Poster Session 4: Case Report [Early Career] (1)

Chair: Dr. Kazuyoshi Ohkawa (Japan)

P-22 10051
A Resected Case of Hepatocellular Carcinoma with Paraneoplastic Syndrome
Dr. Mai Totsuka (Japan)

P-23 10056
A Case of Hepatic Leiomyosarcoma Diagnosed through Autopsy
Dr. Kensho Kubo (Japan)

P-24 10079
A Case of Hilar Bile Duct Carcinoma with Severe Eosinophilia
Dr. Terunao Iwanaga (Japan)

P-25 10109
A Case of Hepatic Reactive Lymphoid Hyperplasia Diagnosed by Post-RFA Biopsy Specimen
Dr. Masaki Kawabata (Japan)

P-26 10111
Cytokine Release Syndrome Caused by the Combination Immunotherapy for Advanced Hepatocellular Carcinoma
Dr. Sae Yumita (Japan)

Poster Session 5: Case Report [Early Career] (2)

Chair: Dr. Yoshiyuki Ueno (Japan)

P-27 10006
A Case of Hepatocellular Carcinoma that could be Radically Resected after Combined Therapy with Lenvatinib and TACE
Dr. Ryo Yano (Japan)

P-28 10035
A Case of Consciously Selected LEN-TACE for Unresectable HCC Combined with Acquired Thrombotic Thrombocytopenic Purpura
Dr. Tsuyoshi Fujioka (Japan)

P-29 10093
Hepatocellular Carcinoma with Long Complete Response after Liver and Lung Resections and Lenvatinib
Dr. Shohe Kobe (Japan)

P-30 10135
Anti-HCV Treatment Using Direct-acting Antivirals during Systemic Immunotherapy for Unresectable Hepatocellular Carcinoma may Contribute to Improving Long-term Prognosis: A Case Report
Dr. Wataru Ueno (Japan)

P-31 10148
A Case of Fatal Immune-Mediated Myocarditis Following Durvalumab and Tremelimumab Combination Therapy (DT) for Multiple Hepatocellular Carcinomas
Dr. Ryo Saito (Japan)

Poster Session 6: Systemic Therapy (1)

Chair: Dr. Toshifumi Tada (Japan)

P-32 10004
Impact of Atezolizumab + Bevacizumab Combination Therapy on Health-related Quality of Life and Relationship with Prognosis in Patients with Advanced Hepatocellular Carcinoma
Dr. Masako Shomura (Japan)

P-33 10038
Cytokine Analysis as a Predictive Biomarker of Response to Treatment with Atezolizumab and Bevacizumab in Advanced Hepatocellular Carcinoma
Dr. Satoshi Kobayashi (Japan)

P-34 10055
Pretreatment Predictors of Response to Combination Therapy with Atezolizumab/Bevacizumab in Advanced Stage Hepatocellular Carcinoma
Dr. Norikazu Tanabe (Japan)

P-35 10141
Clinical Significance of Oncological Resectability Criteria in Patients Treated with Atezolizumab and Bevacizumab
Dr. Yutaka Yasui (Japan)

P-36 10155
Outcomes of Atezolizumab Plus Bevacizumab (Atezo/Bev) Therapy for Hepatocellular Carcinoma (HCC) without Macroscopic Vascular Invasion (MVI) or Extrahepatic Spread (EHS) ~ Focus on Tumor Factors
Dr. Michihisa Moriguchi (Japan)

P-37 10161
CyTOF Reveals Platelet Subtype Changes Predicting the Efficacy of Combined Immunotherapy and Targeted Therapy in Liver Cancer
Dr. Junfeng Lu (China)

Poster Session 7: Systemic Therapy (2)

Chair: Dr. Hidenori Nagai (Japan)

P-38 10059
Predictive Factors for Objective Response Rate in Patients with Unresectable Hepatocellular Carcinoma Treated with Durvalumab plus Tremelimumab Therapy
Dr. Yuki Shirane (Japan)

P-39 10062
Efficacy and Safety of Durvalumab plus Tremelimumab for Advanced Hepatocellular Carcinoma with Esophageal Varices
Dr. Naoshi Odagiri (Japan)

P-40 10069
Effective Monitoring of Durvlumab plus Tremelimumab Therapy Using Tumor Marker
Dr. Issei Saeki (Japan)

P-41 10089
Efficacy and Safety of Immunotherapy for Real-World Elderly Patients with Unresectable Hepatocellular Carcinoma in Japan
Dr. Shun Kaneko (Japan)

P-42 10110
Treatment Efficacy in Durvalumab plus Tremelimumab Therapy for Unresectable Hepatocellular Carcinoma with Previous Immune Check Point Inhibitor
Dr. Nami Mori (Japan)

Poster Session 8: Surgical Resection, Transplantation, and Local Therapy (1)

Chair: Dr. Hiroaki Nagano (Japan)

P-43 10007
Surgical Outcomes of Combined Hepatocellular-Cholangiocarcinoma in Comparison to Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma: A Propensity-Score Matched Analysis
Dr. Hae Won Lee (Korea)

P-44 10030
Short- and Long-term Outcomes of Laparoscopic Liver Resection for Non-alcoholic Fatty Liver Disease-associated Hepatocellular Carcinoma
Dr. Yukihiro Watanabe (Japan)

P-45 10054
Significance of Repeated Laparoscopic Liver Resection for Recurrent HCC after Curative Treatment
Dr. Yuji Iimuro (Japan)

P-46 10057
Attenuation of Hepatic Ischemia-reperfusion Injury Associated with Liver Transplantation by Curcumin in Rodents via Anti-inflammatory Action
Dr. Ekta Yadav (India)

P-47 10082
Current Status of Tumor Ablation in Japan and the Japan Academy of Tumor Ablation (JATA)
Dr. Shuichiro Shiina (Japan)

P-127 10129
Efficacy of HAIC with 3D-CRT for Unresectable Advanced Hepatocellular Carcinoma Complicated by Major Vascular Tumor Thrombosis
Dr. Joji Tani (Japan)

Poster Session 9: Clinical Research of Liver Cancer (1)

Chair: Dr. Michiaki Unno (Japan)

P-48 10008
Clinical Significance of Biliary Invasion at Diagnosis in Barcelona Clinic Liver Cancer Stage B-C Hepatocellular Carcinoma: a Nationwide Cohort Analysis in South Korea
Dr. Sunmin Park (Korea)

P-49 10020
Clinical Characteristics and Prognosis of Hepatocellular Carcinoma Patients without Liver Fibrosis
Dr. Fujimasa Tada (Japan)

P-50 10046
Second-Line Treatment Strategy in Unresectable Hepatocellular Carcinoma after First-Line Atezolizumab Plus Bevacizumab
Dr. Kunihide Mohri (Japan)

P-51 10074
Influence of Gender Differences and Aging on the Clinical Background of Patients with Hepatocellular Carcinoma
Dr. Atsushi Hiraoka (Japan)

P-52 10088
Real World Data of Cabozantinib in Patients with Hepatocellular Carcinoma: Focusing on Dose Setting and Modification
Dr. Hironao Okubo (Japan)

P-53 10136
Comprehensive Analysis of Reaching Radiological Cancer-free Status in Advanced-stage Hepatocellular Carcinoma
Dr. Keisuke Koroki (Japan)

P-54 10152
Real-world Experience of Cabozantinib after Immnotherapy in Patients with Unresectable Hepatocellular Carcinoma
Dr. Kaoru Tsuchiya (Japan)

Poster Session 10: Liver Cirrhosis and Portal Hypertension

Chair: Dr. Keisuke Kakisaka (Japan)

P-55 10022
Hepatocellular Carcinoma is a Prognostic Factor in Patients Treated for Esophagogastric Varices
Dr. Akira Uchiyama (Japan)

P-56 10037
Subharmonic-Aided Pressure Estimation (SHAPE); A New Noninvasive Technique for Diagnosing Portal Hypertension
Dr. Yoshiko Nakamura (Japan)

P-57 10058
Enhancing Bioavailability of Furosemide for the Management of Portal Hypertension Using Self Nano Emulsifying Drug Delivery System
Dr. Pankajkumar Yadav (India)

P-58 10073
Significance of Neutrophil-to-lymphocyte Ratio in Bleeding after Endoscopic Treatment of Cirrhotic Patients with Esophageal Varices
Dr. Kazuto Takahashi (Japan)

P-59 10083
Regional Difference for Morbidity of Liver Cancer and Spread of Ultrasound Elastography in Japan: A Real-world Evidence Using National Database of Health Insurance Claims
Dr. Masahito Nakano (Japan)

P-60 10120
Efficacy and Safety of Avatrombopag
Dr. Rie Goka (Japan)

P-61 10143
The Diagnostic Ability of the Prediction for Hepatocarcinogenesis Using Non-invasive Scoring Systems Including VCTE and CAP in Patients with MASLD/MASH
Dr. Takashi Nishimura (Japan)

Poster Session 11: MASLD

Chair: Dr. Takumi Kawaguchi (Japan)

P-62 10011
Effects of SGLT2 Inhibitors on the Onset of Extrahepatic Cancer in Type 2 Diabetic Patients with MASLD: A Nationwide Database Study in Japan
Dr. Takumi Kawaguchi (Japan)

P-63 10090
Effect of MAFLD on Hepatocarcinogenesis in HBeAg-negative Patients with Undetectable HBV-DNA under NA Therapy: A Multicenter Study
Dr. Keisuke Amano (Japan)

P-64 10116
Modified Forms of Secondary Bile Acid Levels Could be Biomarkers of Hepatocellular Carcinoma Pathogenesis in MASLD Patients
Dr. Yoshimi Yukawa-Muto (Japan)

P-65 10122
Efficacy of Measuring Natural Killer-activating Receptor Ligands to Predict the Pathogenesis of Metabolic Dysfunction-associated Steatotic Liver Disease
Dr. Jun Arai (Japan)

Poster Session 12: Basic Research (1)

Chair: Dr. Naoshi Nishida (Japan)

P-66 10026
Can the Blood Coagulation Factor Von Willebrand Factor be a Predictor of Response to Atezolizumab plus Bevacizumab Combination Therapy for Advanced Hepatocellular Carcinoma?
Dr. Naoki Nishimura (Japan)

P-67 10053
Interaction of PKR and 4.1R Promotes Anchorage-independent Growth of Hepatocellular Carcinoma
Dr. Yusuke Okujima (Japan)

P-68 10108
Hepatoma-derived Growth Factor as a Possible Therapeutic Target for Hepatocellular Carcinoma
Dr. Hirayuki Enomoto (Japan)

P-69 10160
Morphological Architectures of Patient-derived Hepatocellular Carcinoma Organoids with GSK3-beta Expression Dependent Variability According to Lenvatinib Resistance
Dr. Jun Yong Park (Korea)

P-70 10166
Role of Erastin in Intestinal Injury Following Perioperative Liver Transplantation via Ferroptosis in Animals
Dr. Deepika Singh (India)

Poster Session 13: Case Report (1)

Chair: Dr. Tomokazu Kawaoka (Japan)

P-71 10043
A Case of Child-Pugh C with Advanced HCC Treated by a Hepatologist
Dr. Shuntaro Obi (Japan)

P-72 10045
Atezolizumab and Bevacizumab following Stereotactic Body Radiotherapy for Two Patients with Unresectable Hepatocellular Carcinomas with Vp4/Vv3 and Vp3 Macrovascular Invasion
Dr. Satoshi Komiyama (Japan)

P-73 10060
A Case Study of Advanced Hepatocellular Carcinoma Treated with Radiotherapy and Chemotherapy
Dr. Hideo Yoshida (Japan)

P-74 10063
A Case of Hepatocellular Carcinoma with Vp4 Treated with Durvalumab plus Tremelimumab after Lenvatinib plus Hepatic Artery Infusion Chemotherapy
Dr. Mariko Nishioka (Japan)

P-75 10102
Curative Treatment of Two Hepatocellular Carcinoma Cases with Radiofrequency Ablation Following Atezolizumab Plus Bevacizumab
Dr. Kosuke Matsumoto (Japan)

P-76 10145
A Case of Vp4 Hepatocellular Carcinoma Successfully Treated with Hepatic Arterial Infusion Chemotherapy Combined with Radiotherapy (HAIC-RT) and Subsequent Molecular Targeted Therapy
Dr. Hirotoshi Ebinuma (Japan)

P-77 10158
A Case of a Hepatocellular Carcinoma Associated with Autoimmune Hepatitis with Atezolizumab and Bevacizumab Therapy
Dr. Kazuo Tsubura (Japan)

Poster Sessions

Day 2: September 25 (Wednesday) 2024

Room 2 (The Club Fuji C) 16:20-17:20

Poster Session 14: Systemic Therapy [Early Carrer] (2)

Chair: Dr. Teiji Kuzuya (Japan)

P-78 10014
Comparing Clinical Outcomes between PD-L1 and PD-1 Inhibitors Plus Anti-VEGF Antibody Combined with Hepatic Arterial Interventional Therapies in Unresectable HCC: A Single-center, Real-world Study
Dr. Yangxun Pan (China)

P-79 10080
The Efficacy and Safety of Durvalumab + Tremelimumab for Unresectable Hepatocellular Carcinoma
Dr. Aiko Tanaka (Japan)

P-80 10113
Exploring the Safety and Efficacy of Durvalumab Monotherapy for Advanced Hepatocellular Carcinoma Patients Ineligible for Combined Immunotherapy
Dr. Chihiro Miwa (Japan)

P-81 10123
Integrative Deep Learning Framework for Investigating the Role of Tumor-Associated Macrophages in Hepatocellular Carcinoma Metastasis Using Single-Cell Multi-Omics and Spatial Transcriptomics
Dr. Rifaldy Fajar (Indonesia)

P-82 10127
Re-positioning of Hepatic Arterial Infusion Chemotherapy in the Era of Systemic Therapy
Dr. Takahiro Tsuchiya (Japan)

P-83 10139
Significance of Two Patterns of ICI Rechallenge with STRIDE Therapy in Advanced Hepatocellular Carcinoma
Dr. Takuya Yonemoto (Japan)

P-84 10159
Real-World Outcomes of Durvalumab Plus Tremelimumab Combination Therapy (DT Therapy) in Unresectable Hepatocellular Carcinoma: Analysis by Treatment Line and Prognostic Factors
Dr. Naoki Uchihara (Japan)

Poster Session 15: Surgical Resection, Transplantation, and Local Therapy [Early Carrer]

Chair: Dr. Mitsuo Shimada (Japan)

P-85 10013
Challenges and Scope in Deceased Donor Liver Transplantation in Bangladesh: The Dynamics of Ethics, Socio-culture and Religion
Dr. Md Ismail Gazi (Bangladesh)

P-86 10025
Influence of RFA on Liver Reserve Function in Child-Pugh B Patients with HCC within Milan Criteria
Dr. Ayaka Nakamura (Japan)

P-87 10040
Indocyanine Green Applied in Unresectable Hepatocellular Carcinoma after Neoadjuvant Combination Therapy
Dr. Man Luo (China)

P-88 10077
How Far Economics Analysis Does Matter: The Relation of Macroeconomic, Education, and Wealth with Liver Transplantation
Dr. Rosinta H.P. Purba (Indonesia)

P-89 10078
Epidemiology and Risk Factors Relating to Post-Liver Transplantation (LT) in Children
Dr. Lintong H. Simbolon (Indonesia)

P-90 10084
Outcome of Hepatectomy after Systemic Therapy in Hepatocellular Carcinoma: A Japanese Multi-Center Study
Dr. Norifumi Iseda (Japan)

P-91 10128
Efficacy and Safety of Superselective Transarterial Chemoembolization Combined with Systemic Therapy for Unresectable Hepatocellular Carcinoma: A Single-Center Retrospective Cohort Study
Dr. Takuya Watanabe (Japan)

Poster Session 16: Hepatobilialy Malignancy [Early Career]

Chair: Dr. Manabu Morimoto (Japan)

P-92 10003
Targeting Ferroptosis with Polymerized Platinum (IV) Prodrugs Nanoparticles with Everolimus for Enhancing Therapeutic Efficacy on Cholangiocarcinoma
Dr. Yang Chen (China)

P-93 10010
Examination of Interactions Affecting Epithelial-mesenchymal Transition in Intrahepatic Colangiocarcinoma
Dr. Takahiro Haruna (Japan)

P-94 10031
Perioperative Outcomes of Robotic Radical Resection for Gallbladder Cancer: A Single-center Case Series
Dr. Ji-Min Dai (China)

P-95 10068
High-precision Genomic Analysis Using the Molecular Barcoding Method in Liquid Biopsy of Pancreaticobiliary Cancer
Dr. Miho Sakai (Japan)

P-96 10115
Effects of SGLT2 Inhibitors on Cholangiocarcinoma in Cell Lines and an Animal Model
Dr. Daisuke Minowa (Japan)

P-97 10131
Blood CGP Pave the Way for Genomic Therapy in Biliary Tract Cancer ?
Dr. Yoshiki Ogane (Japan)

P-98 10132
The Usefulness of Tissue CGP in Real-World Biliary Tract Cancer Treatment
Dr. Yu Sekine (Japan)

Poster Session 17: Viral Hepatitis [Early Carrer]

Chair: Dr. Masahito Shimizu (Japan)

P-99 10033
A Study on Hepatocellular Carcinoma and Intestinal Microflora in Patients with Chronic Hepatitis B
Dr. Yusuke Tanaka (Japan)

P-100 10034
Clinical Feature of Hepatocellular Carcinoma Patients with Overall Survival (10 Years or More)
Dr. Takuya Matsuda (Japan)

P-101 10036
Treatment Outcomes of Patients with Unresectable Hepatocellular Carcinoma: A Single Center Retrospective Cohort Study
Dr. Christmae M. Solon (Philippines)

P-102 10048
HBV preS1/HBsAg Ratio is a Predictive Marker for the Occurrence of Hepatocellular Carcinoma
Dr. Masanari Kosaka (Japan)

P-103 10157
Promising Antiviral siRNAs for Targeting NS4A and NS5A in Hepatitis C Virus Genotype 1
Dr. Rian Ka Praja (Indonesia)

P-104 10162
The Correlation between Interleukin-6 and the Progression of Chronic Hepatitis B
Dr. Mohamed S. Mahboob Ali (Malaysia)

P-105 10142
An Advanced Predictive System Using Gradient Boosting Machines (GBM) to Forecast Hepatocellular Carcinoma in Patients with Chronic Hepatitis C Virus Infection
Dr. Prihantini Prihantini (Indonesia)

Poster Session 18: Case Report [Early Career] (3)

Chair: Dr. Kazuhiro Nouso (Japan)

P-106 10103
A Case of Atezolizumab-Bevacizumab Combination Therapy with Good Long-Term Prognosis Despite Prolonged Bevacizumab Withdrawal
Dr. Fumiya Suzuki (Japan)

P-107 10134
A Case of Hepatocellular Carcinoma with Bone Metastasis Achieved Complete Response Using Stereotactic Radiotherapy and Lenvatinib, Following Anti-PD-L1 Antibody-induced Psoriasis-like Dermatitis
Dr. Chikako Nagao (Japan)

P-108 10146
A Case of Hepatocellular Carcinoma with Multiple Pulmonary Metastatic Recurrences at Distant Stage after Radical Cure
Dr. Akihiko Nishimura (Japan)

P-109 10147
Remarkable Response to Atezolizumab plus Bevacizumab Therapy after Psuedo-progression, Followed by Phenotypic Change in Conversion Surgery: A Unique Case of Hepatocellular Carcinoma
Dr. Midori Sawada (Japan)

P-110 10169
A Cholangiolocellular Carcinoma Case Showing Slow Tumor Growth and Marked Intratumoral Lymphocyte Infiltration, with a Favorable Outcome
Dr. Ayaka Gamo (Japan)

Poster Session 19: Systemic Therapy (3)

Chair: Dr. Hayato Hikita (Japan)

P-111 10001
Survey of Systemic Drug Therapy for Unresectable Hepatocellular Carcinoma in Non-designated Regional Cancer Treatment Hospital in Japan
Dr. Hidehiro Kamezaki (Japan)

P-112 10044
Hepatic Dysfunction in 879 ICI-treated Patients; Does Referral to a Hepatologist Improve OS?
Dr. Kaori Matsumoto (Japan)

P-113 10061
Atezolizumab plus Bevacizumab Shows PFS Benefit in mALBI Grade 2 HCC
Dr. Shunji Watanabe (Japan)

P-114 10075
Results of Atezolizumab Combined with Bevacizumab for Advanced Hepatocellular Carcinoma in Vietnamese Patients
Dr. Hang T. Hoang (Viet Nam)

P-115 10099
Assessment of Macrovascular Invasion in Advanced Hepatocellular Carcinoma: Clinical Implications and Treatment Outcomes with Systemic Therapy
Dr. Masanori Inoue (Japan)

P-116 10107
A Retrospective Analysis of Liver Volume Decrease in Advanced Hepatocellular Carcinoma Patients Treated with Atezolizumab plus Bevacizumab and Lenvatinib
Dr. Tomoharu Yamada (Japan)

P-117 10121
Diagnosis Triggers and Outcomes in Patients Treated with Atezolizumab/Bevacizumab as Initial Treatment for Hepatocellular Carcinoma
Dr. Teiji Kuzuya (Japan)

Poster Session 20: Systemic Therapy (4)

Chair: Dr. Tatehiro Kagawa (Japan)

P-118 10027
Systemic Therapy for Unresectable HCC Combination with TACE (Lenvatinib or Atezolizumab/Bevacizumab)
Dr. Ryu Sasaki (Japan)

P-119 10100
Efficacy of Lenvatinib + New FP Combination Therapy in the Treatment of Unresectable Advanced Hepatocellular Carcinoma
Dr. Susumu Maruta (Japan)

P-120 10124
Combining On-demand Locoregional Treatment for Drug-resistant Lesions during Atezolizumab and Bevacizumab Therapy in Unresectable Hepatocellular Carcinoma
Dr. Tasuku Nakabori (Japan)

P-121 10138
Effectiveness of Immune Checkpoint Inhibitor Therapy with Locoregional Therapy Versus ICI Alone in Unresectable Hepatocellular Carcinoma: A Retrospective Analysis
Dr. Yasuhide Motoyoshi (Japan)

P-122 10149
Is Lenvatinib Resumption Necessary after Lenvatinib-TACE Combination Treatment ?
Dr. Rie Sugimoto (Japan)

P-123 10165
Effect of Radiofrequency Ablation on the Therapeutic Efficacy of Atezolizumab/Bevacizumab Combination Therapy
Dr. Masahiko Tameda (Japan)

Poster Session 21: Surgical Resection, Transplantation, and Local Therapy (2)

Chair: Dr. Shuntaro Obi (Japan)

P-124 10029
Carbon-ion Radiotherapy for Hepatocellular Carcinoma 4 cm or Larger
Dr. Tetsuro Isozaki (Japan)

P-125 10081
Ablation Training Program for Liver Tumors at Juntendo
Dr. Shuichiro Shiina (Japan)

P-126 10098
LI-RADS CT/MRI Radiation Treatment Response Assessment Version 2024: Evaluation after Transarterial Radioembolization for Hepatocellular Carcinoma
Dr. Sunyoung Lee (Korea)

P-128 10151
Clinical Outcomes with Stereotactic Body Radiation Therapy in Patients with Hepatocellular Carcinoma
Dr. Puja Sahai (India)

Poster Session 22: Clinical Research of Liver Cancer (2)

Chair: Dr. Hirayuki Enomoto (Japan)

P-129 10071
Efficacy of the GFAD Index as a New Indicator for the Early Diagnosis of Non-Viral Hepatocellular Carcinoma
Dr. Akiyo Ishiguro (Japan)

P-130 10087
The Association between the Prognoses and Systemic Chemotherapy According to the Oncological Conditions in Patients with Colorectal Liver Metastases
Dr. Nozomu Sakai (Japan)

P-131 10095
Quality of Life in Patients with Hepatobiliary Cancers
Dr. Asmin Valiyagath (India)

P-132 10097
Does Transcatheter Arterial Chemoembolization for Liver Metastasis in Neuroendocrine Tumors Reduce Hepatic Reserve?
Dr. Asako Nogami (Japan)

P-133 10101
Clinical Outcome of GCD Therapy for Unresectable Intrahepatic Cholangiocarcinoma
Dr. Hiroki Inada (Japan)

P-134 10105
Etiological Transitions in Patients with Liver Cirrhosis and Hepatocellular Carcinoma: a Single-center Study from an Institution Located in a District with a High Prevalence of Viral Hepatitis
Dr. Hirayuki Enomoto (Japan)

P-135 10140
Atezolizumab plus Bevacizumab for Combined Hepatocellular Cholangiocarcinoma
Dr. Tomoyuki Satake (Japan)

Poster Session 23: Viral Hepatitis

Chair: Dr. Norio Akuta (Japan)

P-136 10070
A Novel Hepatitis Delta virus (HDV) in Vitro Carcinogenesis Model
Dr. Shinya Sato (Japan)

P-137 10091
The Prognosis of Hemodialyzed Patients with Hepatitis C Treated by Direct Acting Antivirals
Dr. Hitoshi Takagi (Japan)

P-138 10094
Comprehensive RNA-seq Analysis of HCV-infected Cells and Specimens from Patients with Liver Cancer after HCV Eradication to Elucidate Liver Carcinogenesis
Dr. Katsuya Nagaoka (Japan)

P-139 10096
Epidemiology of Liver Disease in Kerala: A Retrospective Study
Dr. Sabin Katpattil (India)

Poster Session 24: Basic Research (2)

Chair: Dr. Tsutomu Masaki (Japan)

P-140 10021
Oncolytic Activity of a Chimeric Influenza A Virus Carrying a Human CTLA4 Antibody in Hepatocellular Carcinoma
Dr. Penghui Yang (China)

P-141 10024
Cabozantinib Prevents the Progression of Metabolic Dysfunction-associated Steatohepatitis by Inhibiting the Activation of Hepatic Stellate Cell and Macrophage and Attenuating Angiogenic Activity
Dr. Takuya Matsuda (Japan)

P-142 10028
Extracellular Vesicles-mediated Mutant β-catenin Transfer from Hepatocyte Activates Hepatic Stellate Cells in Tumor Microenvironment
Dr. Yu Ota (Japan)

P-143 10032
Tumor-derived CCL15 Regulates RNA m6A Methylation in Cancer-associated Fibroblasts to Promote Hepatocellular Carcinoma Growth
Dr. Yueguo Li (China)

P-144 10112
A Near-infrared-modulated System Enabling Efficient Delivery of Glucose Derivative as a New Therapeutic Strategy for Liver Cancer
Dr. Sohji Nishina (Japan)

P-145 10164
Chemoprotective Effect of Crocetin-Dextrin Nano-Formulation against N-Diethylnitrosamine Induced Hepatocellular Carcinoma in Rats via Mitochondrial Apoptosis and PI3K/Akt/mTOR Signaling Pathways
Dr. Vikas Kumar (India)

P-146 10168
The Whole Genome and RNA Sequence Analysis on the Hepatocellular Carcinoma Derived from the Patients with Fontan-associated Liver Disease
Dr. TaijiYamazoe (Japan)

Poster Session 25: Basic Research (3)

Chair: Dr. Makoto Chuma (Japan)

P-147 10009
Development of a Small Animal Model for Fatty Liver-related Hepatocarcinogenesis Research
Dr. Daiki Miki (Japan)

P-148 10039
Withdrawn

P-149 10047
Inhibitory Effects of Putrescine on Metabolic Dysfunction-associated Steatohepatitis in Mice
Dr. Erdenetsogt Dungubat (Japan)

P-150 10119
Exploring the Link Between Mitochondrial ROS, Peroxiredoxin V, and Liver Fibrosis in Metabolic Associated Fatty Liver Disease
Dr. Hyun Ae Woo (Korea)

P-151 10167
Efalizumab Modulates HAT1 and Increases IL-9 to Induce Ferroptosis and CD8+ T Cell Immunological Activity in Hepatocellular Carcinoma
Dr. Manvendra Singh (India)

P-152 10170
Invasive Hepatic Stellate Cell Shapes Immunovascular Landscape of Hepatocellular Carcinoma
Dr. Michitaka Matsuda (Japan)

P-159 10171
Investigation of TEAD Inhibitor for Hepatocellular Carcinoma Treatment
Dr. Yoshinobu Saito (Japan)

Poster Session 26: Case Report (2)

Chair: Dr. Takahiro Yamasaki (Japan)

P-153 10023
Myositis Induced by an Immune Checkpoint Inhibitor in a Hepatocellular Carcinoma Patient with Primary Biliary Cirrhosis: A Case Report
Dr. Naoya Tsuzuki (Japan)

P-154 10067
A Case of Unresectable Hepatocellular Carcinoma Complicated by Cerebral Hemorrhage after Combined Therapy with Atezolizumab and Bevacizumab
Dr. Tamami Abe (Japan)

P-155 10072
A Case of Duodenal Bleeding from Invasion of Lymph Node Metastasis during Combination Therapy with Atezolizumab and Bevacizumab for Hepatocellular Carcinoma
Dr. Kyoko Hoshikawa (Japan)

P-156 10076
A Case of Hepatic Hemangiosarcoma Followed by Long-term Imaging
Dr. Takayuki Kogure (Japan)

P-157 10106
A Case of Hepatic Focal Nodular Hyperplasia after Liver Transplantation
Dr. Kenichi Nakamura (Japan)

P-158 10137
A Case of Scirrhous Hepatocellular Carcinoma Discovered after Combined Immunotherapy for Hepatocellular Carcinoma
Dr. Yuta Maruki (Japan)

Memo

APASL Oncology 2024 Chiba

"Genomics Meets Immunology:
Interdisciplinary Approach for Liver Cancer"

Abstracts

Special Lectures

Special Lecture 1

Dr. Lai Wei
Dean and Professor,
Hepatopancreatobiliary Center, Beijing Tsinghua Changgung Hospital,
School of Clinical Medicine, Tsinghua University, Beijing,
China

Prevention of Primary Liver Cancer, China Perspective

In the past 5 years, the average annual number of new cases of primary liver cancer was 995,000 cases worldwide, with 732,000 cases in Asia and 423,000 cases in China, accounting for 73.6% and 42.5% worldwide, respectively. Liver cirrhosis is a major risk factor for HCC. Chronic HBV infection is the main cause of HCC in China, accounting for approximately 86%. Other causes include chronic HCV infection, alcohol-related liver disease (ALD) caused by long-term excessive drinking, NAFLD, T2DM, and long-term consumption of afatoxin-contaminated food.

The strategy for secondary prevention included AFP as preferred serological marker for early HCC surveillance, and combined detection with PIVKA-II and AFP-L3 to improve the diagnostic accuracy For patients with negative or mildly elevated serum AFP, combined detection of PIVKA-II and AFP-L3, based on the dynamic change of serum AFP levels, can improve the diagnostic accuracy of early HCC. Routine abdominal ultrasound is the main imaging method for monitoring the HCC risk population. CEUS can assist in diferentiating tumor features. Plain and enhanced liver CT can be used for the diferential diagnosis and monitoring of nodules>1 cm in diameter. Multimodal MRI (plain, DWI, and enhanced) is the most sensitive imaging method for the surveillance of HCC. It can detect tumors≤ 1 cm in diameter and is used for HCC surveillance in nodular cirrhosis and to diferentiate the features of suspicious nodules found by ultrasound. Hepatocyte-specifc GdEOB-DTPA-enhanced MRI can improve the detection rate of HCC with the diameter≤1 cm and is a valuable clinical means to diferentiate benign hyperplastic nodules, precancerous lesions, and early HCC.

The strategy for tertiary secondary prevention included 1) risk stratifcation for recurrence after curative treatment of HCC, 2) surveillance protocol for HCC recurrence, 3) treatment for etiologically related diseases of HCC.

Special Lecture 1

Dr. Shiv Kumar Sarin
Professor of Eminence,
Department of Hepatology, Chancellor,
Institute of Liver and Biliary Sciences, New Delhi,
India

Management of Portal Hypertension and its complications in HCC: A 2024 update

Hepatocellular carcinoma (HCC) is rapidly increasing and it most often develops in patients with cirrhosis. MAFLD and alcohol related HCC are increasing rapidly in Asia. Increasing liver stiffness and rise in portal pressure increase the risk of development of HCC. Besides the stage of liver disease - Childs' A, B or C; the degree of portal hypertension (PH) does contribute to the outcome of HCC patients. Acute variceal bleed (AVB), ascites, low platelet count and portal vein thrombosis (PVT) due to PH pose major challenges.

AVB in a cirrhosis with HCC patient portends bad outcome, the survival is reduced to a median of 5 months compared with 38 months in cirrhosis without HCC. The presence of portal vein tumor thrombosis is associated with a higher risk of AVB, which is often difficult to control. Careful planning should be done to prevent AVB in such patients. The overall survival of Child-Pugh A patients without CSPH was 70% at 5 years, while it dropped to 25-50% in patients with CSPH.

Conventionally, for hepatic resection, a platelet count of >100,000 and an HVPG of <12 mmHg is recommended for preventing decompensation and better outcome. With the introduction of non-invasive tests, we may use a liver stiffness ≤15 kPa and a platelet count of ≥ 150,000 /cmm to exclude and LSM ≥ 25 kPa and spleen stiffness measurement (SSM) of >50 to rule in CSPH. However, patients, due to the presence of PVT. An UGI endoscopy should therefore be performed in all HCC patients. Intervention procedures such as TACE and TARE are likely to increase the portal pressure and result in hepatic decompensation. Rapid progression in the size of EVs associated with AVB has been reported in infiltrative HCC and in patients with macro-vascular invasion.

The TIPS placement is a good option for managing refractory bleed and progressive ascites in HCC patients. However, the fear of HCC progression and tumour spread to lungs and distant sites remains. TIPS may also influence the outcomes and safety of locoregional treatment for HCC, which remains uncertain. In a recent series of 640 HCC patients, the liver explants did not outline higher HCC occurrence. In fact, TIPS placement can improve liver function in patients with ascites and allow them to access locoregional treatment.

Hepatic sinusoidal obstruction syndrome was also noted after nivolumab treatment. Increase in size of varices has been reported on atezolizumab-bevacizumab treatment. In the Imbrave 150 study, bleeding events were more frequently observed with the combination of bevacizumab and atezolizumab than with sorafenib (25.2% vs. 17.3%), including 2.4% and 0.6% of AVB cases. It is not clear whether band ligation should be offered as primary prophylaxis or for those with contraindications/intolerance to NSBBs. Certainly, we should offer band ligation for secondary prophylaxis. As of now, we should stop bevacizumab after AVB. The results of other phase 3 studies using TKIs in combination with immunotherapy and their impact on PHT are pending.

Portal vein tumor thrombosis (PVTT) is present in 10%-40% of HCC at the time of diagnosis, and is an adverse prognostic factor. Patients with PVTT usually have an aggressive disease course, poor hepatic functional reserve, limited treatment options and higher recurrence rates. Among untreated HCC patients with PVTT, the median overall survival has been reported as 2 to 4 months. The PVTT results in disordered hepatic and portal blood flow and associated impairment of liver function, heat-sink effects of blood flow in the area of PVTT, risk of recurrence and spread of tumor along the blood vessels. Non-tumor PV thrombosis is also not uncommon in an HCC patient and needs to be investigated. High dose vitamin K3 has been shown to reduce PIVKA II levels and repermeation.

Low platelet counts often pose challenges for undertaking local ablative therapies. TOTEM based corrections, platelet transfusion and TPO agonists should be used in patients with platelet counts <50,000 /cmm. Since there are no clear guidelines, we propose that all patients of HCC with PVT should be placed on beta-blockers as primary prophylaxis for variceal bleeding. In those with active bleeding, variceal band ligation or cyanoacrylate glue therapy should be offered. In those with uncontrolled bleed, or those with refractory ascites, a TIPS stent placement should be considered. Protocols are needed for restarting immunotherapy and TKIs after a variceal bleed. A personalized and multidisciplinary management is desirable for achieving 50% two years survival in patients of HCC and portal hypertension.

Special Lecture 2

Dr. Jazag Amarsanaa
Founder, Head Investigator of "Mongolian Genome Project",
Chairman, Board of Directors of Otoch-Manramba Medical University,
Happy Veritas Hospital Advisor,
Mongolia

HCC Etiology, Incidence, Diagnosis, Management and Survival in Mongolia, Update of A-HOC Studies

Jazag Amarsanaa, Baatarkhuu Oidov, Erdenebayar Gonchig, Enkhbold Chinbold,
Erkhembayar Dimaa, Yumchinserchin Narangerel, Bolortsetseg Batdelger,
Myagmar-Ochir Ragchaasuren, Masao Omata

Liver cancer incidence in Mongolia is 63.2 per 100,000 population, or 6.5 times higher than the world average.

During the last 12 years, 26,543 cases of liver cancer were registered between 2010 and 2022, which accounts for 36.3% of all malignancies detected in Mongolia, mortality-wise 21,312 deaths were caused by HCC, 42.2% of all cancer deaths.

The 12 years cumulative survival rate of HCC is 19.8%.

0.1% of HCC was detected in situ, 4.4% are in stage 1, 20.1% are in stage 2, 39.5% are in stage 3, and 39.2% are in stage 4.

Currently Mongolia is an active participant of A-HOC studies, supported by APASL.

If the liver cancer in Mongolia is classified by regions, it is 27.2% in the Western region, 18.3% in the Central region, 24.8% in the Gobi region, and 31.2% in the Eastern region.

Tests and equipment currently used to detect liver cancer in Mongolia: US, dynamic CT, EOB-MRI, Pathology, Angiography, tumor markers AFP, Pivka-ll, L-3

Treatment of liver cancer in Mongolia: liver transplantation, hepatectomy, RFA/MWA, TAE/TACE, Sorafenib, Lenvatinib, Atezolizumab/Bevacizumab

The peak age of liver cancer in Mongolia is 61-66 years for women and 56-60 years for men. Also, the youngest age at which liver cancer was diagnosed was 32 years for men and 34 years for women.

A-HOC reveals 37.6% of HCCs are primary and 63.4% are recurrent.

Etiology of HCCs are 18% is of non-viral origin, 7% of alcoholic origin, and 75% are of viral origin, but this trend is slowly changing.

Special Lecture 2

Dr. Masao Omata
Gastroenterology, University of Tokyo,
Yamanashi Central & Kita Hospitals,
Japan

Hepatology in Asia: Navigating the Landscape of Liver Diseases (HCC)

With 54 years of clinical experiences (6 at US, 16 at Chiba U, 17 at U Tokyo and 15 at YCH), suggestions could be made for the future.

YCH is principal cancer and genome center for patients with all types of malignancies where we are obliged to prospectively follow every single case since 2006. So far, we have enrolled and prospectively followed 30,000 cases including 1,080 HCC till 2023. Etiologies were simply classified into *Viral* (type B/ HBsAg positive, type C/HCV Ab positive) and *Non-Viral* (metabolic, alcoholic, autoimmune and others). Etiologic profile shift was expressed as percentile and by absolute numbers of corresponding etiologies.

Dynamics of etiological changes was shown in Figure. It is so obvious to see the reversion of *Virals* to *Non-Virals*. In recent years, we saw only a few cases of B-Viral and C-viral HCCs, making *Non-Viral* as nearly 80% of all.

Last year, we started A-HOC (APASL Hepatology Oncology Consortium) Study which enabled us to oversee the changes of practice in Asia including preventions, diagnosis and treatment of HCC. By this A-HOC study, we are able to navigate the landscape of liver disease, HCC in particular, and this may become one of the key functions of APASL.

Memo

APASL Oncology 2024 Chiba

"Genomics Meets Immunology:
Interdisciplinary Approach for Liver Cancer"

Abstracts

Sessions

Dr. Yujin Hoshida
Internal Medicine,
University of Texas Southwestern,
USA

Deciphering Liver Cancer: Molecular Pathways, Mechanisms, and Identifying High-Risk Groups for Carcinogenesis and Recurrence

The limited efficacy of existing therapies indicates the importance of preventive interventions to substantially improve the poor prognosis of patients with liver cancer, including hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). Prevention of HCC in chronic liver disease patients remains a challenge with the evolving etiological landscape, particularly the sharp increase in metabolic dysfunction-associated steatotic liver disease (MASLD) accompanied with the obesity epidemic. The wide-spread use of new-generation antivirals for hepatitis C virus (HCV) and hepatitis B virus (HBV) infection has substantially reduced, but not eliminated, HCC risk, and posed new challenges to identify a subset of patients who still need preventive interventions after viral control. In addition, globally increasing alcohol intake over the COVID-19 pandemic has led to the rise of alcohol-associated liver disease (ALD). With the shifting landscape of etiological/risk factors and the advent of new therapeutic agents/modalities, there are unprecedented opportunities to refine the strategies of HCC prevention at all three levels, i.e., primary, secondary, and tertiary prevention. In primary prevention (before exposure to the risk factors), public health policies such as universal neonatal HBV vaccination continue to show supporting data. Secondary prevention (after and/or with active exposure to the risk factors) encompasses regular HCC screening and chemoprevention. Emerging HCC risk stratification and detection biomarkers and imaging modalities may enable individual risk-based personalized and cost-effective HCC screening. Accumulating retrospective and epidemiological studies continue to suggest potential utilities of statins, anti-diabetics, and anti-inflammatory agents, many of which are relevant to MASLD and metabolic disorders, may serve as HCC chemoprevention, some of which are being evaluated in prospective clinical trials. Computational and experimental studies have also identified potential new chemopreventive strategies targeting diverse molecular, cellular, and systemic targets. Tertiary prevention (after receiving curative treatment of the first HCC) combination immuno-oncology agents in the form of neo/adjuvant therapies after surgical/ablative therapies with curative intent.

Dr. Tatsuhiro Shibata
Professor,
Laboratory of Molecular Medicine, Human Genome Center,
The Institute of Medical Science, The University of Tokyo,
Chief, Division of Cancer Genomics, National Cancer Center,
Japan

Leveraging Genomic Insights to Advance Liver Cancer Diagnosis and Treatment

Hepatocellular carcinoma (HCC) is common in East Asia, including Japan. Compilation and re-analysis of 1,340 multi-ethnic HCC genomes, the largest cohort ever reported, identified a comprehensive landscape of HCC driver genes comprising three core drivers (TP53, TERT and WNT signaling) and a combination of rare alterations in different cancer pathways. Consistent with their heterogeneous epidemiological backgrounds, mutational signatures and combinations of non-core driver genes within these cancer genomes were found to be complex. Integrative analyses of multi-omics data identified molecular classifications of these tumors associated with clinical outcome and enrichments of potential therapeutic targets, including immune checkpoint molecules. The translation of comprehensive molecular genetic analyses, together with further basic research and international collaborations, is highly anticipated for the development of precise and better treatments, diagnosis and prevention of these tumor types.

Dr. Hayato Nakagawa
Department of Gastroenterology and Hepatology,
Mie University,
Japan

Liver Metabolism as a Driver of Hepatocarcinogenesis: Emerging Concepts and Future Directions

In MASLD-related hepatocellular carcinoma (HCC), there is a histological subtype known as steatohepatitic HCC (SH-HCC), characterized by fat accumulation in cancer cells. Our comprehensive metabolomic analysis of MASLD-related liver cancer revealed an accumulation of acylcarnitine and decreased expression of CPT2, leading to the suppression of fatty acid β-oxidation (FAO). This appears to be an adaptive response to the lipid-rich environment of MASLD. In addition, β-catenin mutation plays a key role in the status of FAO. On the other hand, lipid metabolism may have impact on anti-tumor immunity, and fat accumulation in HCC cells reportedly suppresses anti-tumor immunity. When classifying metabolic subtypes based on lipid metabolism, those with reduced FAO show higher immune cell infiltration and potential efficacy of immune checkpoint inhibitor (ICI), whereas those with enhanced FAO may respond less effectively to ICIs but may benefit more from transarterial chemoembolization.

The process of carcinogenesis from MASLD involves dynamic changes in lipid metabolism, which also informs our attempts at personalized medicine based on these metabolic shifts. In this presentation, I will introduce our research and efforts in personalizing treatment strategies for MASLD-related hepatocellular carcinoma, emphasizing the adaptation of cancer cells to their metabolic environment and the implications for treatment selection.

Dr. Yosuke Hirotsu
Manager, Chief Researcher,
Genome Analysis Center,
Yamanashi Central Hospital,
Japan

Unraveling the Complexity of Tumor Heterogeneity in Hepatocellular Carcinoma: Intra-tumoral and Inter-tumoral Perspectives

Yosuke Hirotsu[1] and Masao Omata[2,3]
[1] Genome Analysis Center, Yamanashi Central Hospital
[2] Department of Gastroenterology, Yamanashi Central Hospital
[3] University of Tokyo

Hepatocellular carcinoma (HCC) exhibits significant heterogeneity, challenging effective treatment strategies. This study investigates both intra-tumoral and inter-tumoral genetic variations in HCC to guide targeted therapies. Intra-tumoral analysis: We performed multi-regional sequencing on 68 HCC nodules from 26 patients using a 72-gene panel related to HCC. Tumor phylogeny and cellular prevalence were estimated using mutational profiles. Trunk mutations were found in HCC samples, with TERT and TP53 predominantly identified as trunk mutations. CTNNB1, NFE2L2, and chromatin remodeling genes were mainly observed as branch mutations. Phylogenetic analysis revealed diverse evolutionary patterns for different mutated clones, suggesting ancestor tumor clones differentiated into various phenotypic compartments. Inter-tumoral analysis: We profiled 193 tumor lesions (82 synchronous, 111 metachronous) from 68 patients with multifocal HCC using a 72-gene panel. Synchronous tumors exhibited an average of 3.1 somatic mutations and 0.7 actionable mutations per lesion, while metachronous tumors showed 4.0 and 1.0, respectively. Metachronous tumors displayed significantly more aberrant signaling pathways, including Wnt/β-catenin and KEAP1/NRF2. Notably, 45.6% of patients showed divergent actionable mutations across lesions, potentially influencing treatment selection for individual tumors. This comprehensive study reveals substantial intra- and inter-tumoral heterogeneity in HCC. The identification of trunk mutations as potential therapeutic targets and the divergence in actionable mutations across lesions emphasize the need for personalized treatment strategies based on comprehensive molecular profiling in HCC management.

Dr. Mina Komuta
Pathology Department,
International University of Health and Welfare,
School of Medicine, Narita Hospital,
Japan

Carcinogenesis and Its Evolution of Primary Liver Cancers from a Pathological Perspective

Primary liver cancers mainly include hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (iCCA), and combined hepatocellular-cholangiocarcinoma (cHCC-CCA).
These tumors, particularly HCC, commonly develop in the context of chronic liver diseases, which may result from metabolic or alcohol-related steatotic liver diseases, as well as viral hepatitis B or C. Additionally, iCCA can arise from chronic biliary inflammatory conditions such as primary biliary cholangitis and hepatolithiasis.
Despite the different aetiologies associated with these tumours, chronic liver damage—characterized by inflammation and fibrosis—is a critical factor in hepatocarcinogenesis. Persistent hepatocellular and/or cholangiocellular injury eventually creates a pro-oncogenic environment.
Importantly, the process and pattern of liver injury vary depending on the aetiology, which in turn influences tumour characteristics. For example, multi-step hepatocarcinogenesis is commonly observed in viral hepatitis C, but its frequency is lower in steatohepatitis-related HCC. Recent studies also suggest that the pattern of recurrence after HCC surgery differs according to the underlying aetiology.
Similar distinctions are seen in iCCA. The characteristics of iCCA differ significantly depending on its cell-of-origin. Large duct-type iCCA, originating from mucin-producing cholangiocytes, tends to have aggressive clinicopathological features and is often associated with KRAS and SMAD3 mutations. In contrast, small duct-type iCCA, arising from mucin-negative cholangiocytes, presents with less aggressive phenotypes and is associated with actionable mutations such as IDH1/2 mutations and/or FGFR2 fusions.
The clinical and molecular presentation of cHCC-CCA remains obscure due to inconsistencies in diagnostic criteria.
In my presentation, I will summarize the current understanding of the pathological and molecular features of primary liver cancers and their carcinogenesis. I will also highlight the pathomolecular features of chronic liver diseases, including steatotic liver diseases and viral hepatitis, emphasizing the importance of recognizing different aetiologies to understand hepatocarcinogenesis.

Dr. Arndt Vogel
Professor of Medicine, University of Toronto, Longo Family Chair in Liver Cancer Research Division of Gastroenterology and Hepatology, Toronto General Hospital Medical Oncology, Princess Margaret Cancer Centre Toronto General Hospital Research Institute, Schwartz Reisman Liver Research Centre Institute for Medical Science, Canada

Landscape of Western HCC Guidelines

Hepatocellular carcinoma (HCC) presents a significant global health challenge, marked by rising incidence and mortality rates. For those with early and intermediate-stage disease, a variety of local therapies, including surgical (resection and transplantation), interventional (radiofrequency ablation [RFA] and microwave ablation [MFA]), intra-arterial (selective internal radiation therapy [SIRT] and transarterial chemoembolization [TACE]), and radiation approaches (brachytherapy and stereotactic body radiation therapy [SBRT]) have been firmly established in clinical practice. Systemic therapies are utilized in approximately 50% to 60% of HCC patients.

In the context of advanced HCC, first-line treatment options currently consist of five distinct regimens, while second-line and subsequent therapies offer up to five alternatives in Western countries. In China, three additional molecular therapies have demonstrated superior efficacy compared to sorafenib. The expanding array of effective treatments has resulted in a higher number of patients achieving cure and a notable increase in median overall survival (OS) for advanced HCC patients, from 8 months in the placebo group to 2 years with immune checkpoint inhibitor-based combinations, which are now the standard of care for first-line treatment.

These therapeutic regimens are endorsed by guidelines from both U.S. (American Association for the Study of Liver Diseases [AASLD], American Society of Clinical Oncology [ASCO], National Comprehensive Cancer Network [NCCN], and American Gastroenterological Association [AGA]) and European (European Society for Medical Oncology [ESMO] and European Association for the Study of the Liver [EASL]) organizations. However, the rapid publication of new data and studies achieving their primary endpoints, coupled with limited high-level evidence supporting recommendations in specific clinical scenarios, have hindered the development of a definitive treatment sequence or flowchart.

In my presentation, I will summarize the current guidelines and treatment algorithms as outlined by the key Western HCC guidelines.

Dr. George K. K. Lau
Humanity and Health Clinical Trial Center,
Humanity and Health Medical Group, Hong Kong SAR, China
Zhongshan Hospital, Fudan University, Shanghai, China

The Latest APASL Clinical Practice Guideline on Systemic Therapy for Hepatocellular Carcinoma

In Asia-Pacific region, hepatocellular carcinoma is a serious health threat attributing to over 600,000 deaths each year and account for over seventy percent of global cases. Clinically, the major unmet needs are recurrence after curative intent surgery or local ablation and disease progression in those with hepatocellular carcinoma not eligible for resection or failed locoregional therapy. In the recent few years, new targeted therapy and immune-checkpoint inhibitors have been registered as systemic therapy to address these issues. Notably, new form of systemic therapy either as first-line or second-line therapy for unresectable hepatocellular or not eligible for locoregional therapy, are now available. The gravity of chronic hepatitis B and C as aetiology of hepatocellular carcinoma in Asia-Pacific region, is of great relevance as the response to immune-checkpoint inhibitors has been suggested to be much higher, as compared to targeted therapy. New data is also emerging with the use of systemic therapy to prevent hepatocellular carcinoma recurrence after curative intent resection or local ablation therapy and to retard disease progression after locoregional therapy. In the future, further implementation of immune-checkpoint inhibitors and other form of immunotherapy are expected to bring a new paradigm to the management of hepatocellular carcinoma. New insight and hence management strategy related to immune-mediated adverse events with the use of immunotherapy is also enabling one to optimize therapeutic approach to our patients with hepatocellular carcinoma. The purpose of this clinical practice guideline is to provide an up-to-date recommendation based on clinical evidence and experience from regarded Asia-Pacific key opinion leaders in the field of hepatocellular carcinoma. Three key questions will be addressed, namely (1) which patients with hepatocellular carcinoma should be considered for systemic therapy? (2) which systemic therapy should be used? and (3) how should a patient planned for immune checkpoint-based systemic therapy be managed and monitored?

Dr. Hitoshi Mochizuki
Genome Analysis Center /
Gastroenterology, Yamanashi Central Hospital,
Japan

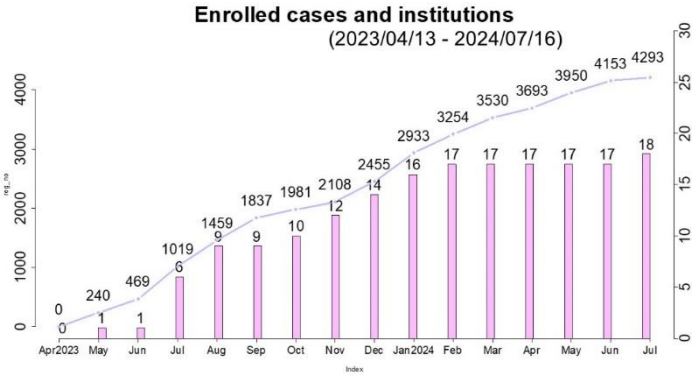
A-HOC Start-up and Current State

The A-HOC (APASL Hepatology/Oncology Consortium) study is planned to enter 10,000 cases from countries and regions in the Asia-Pacific region that are important for the development of APASL guidelines, to understand the actual situation in each country and the efficacy of new therapeutic agents such as immune checkpoint inhibitors.

This study began in January 2023 with President Omata as the principal investigator, and the first IRB was approved in March 2023.

By July 2024, 18 institutions, in 7 countries and regions (JPN, CHN, TUR, IDN, MNG, TWN, KOR) have participated in the study, and 4650 cases have been enrolled.

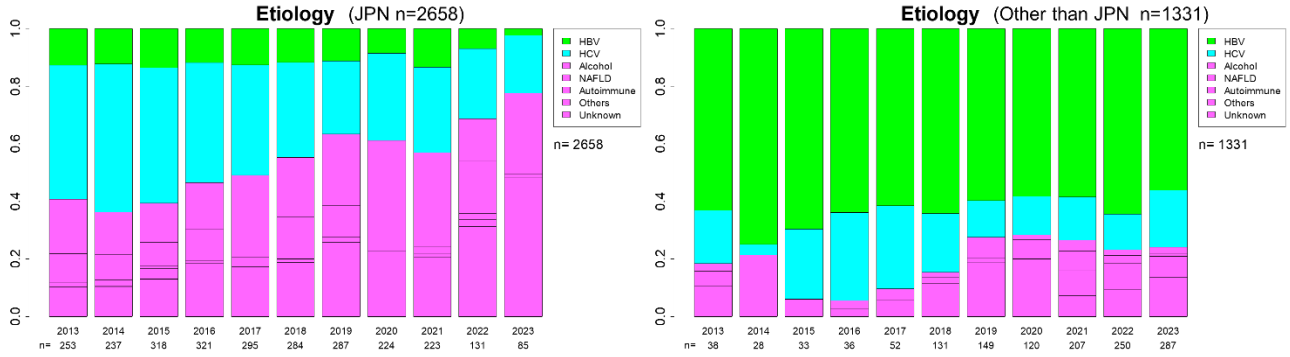
Institutions (In order of IRB approval date)
Yamanashi Central Hospital (JPN)
Matsudo City General Hospital (JPN)
Okayama University (JPN)
Kagawa University (JPN)
Chiba University (JPN)
Yamagata University (JPN)
Humanity & Health Medical Group (CHN)
Teikyo University (JPN)
The University of Tokyo (JPN)
Nagasaki Medical Center (JPN)
Beijing Tsinghua Changgung Hospital (CHN)
Gazi University (TUR)
Juntendo University (JPN)
Dharmais National Cancer Center (IDN)
Happy Veritas Hospital (MNG)
Mochtar Riady Comprehensive Cancer Center(IDN)
Taipei Veterans General Hospital (TWN)
Seoul National University Hospital (KOR)



This study uses REDCap（Research Electric Data Capture）, which is highly confidential and is a revolutionary clinical research support tool that is becoming a global standard in academic medical research.

In addition, many registered researchers can view the status of their data in real time using the provided functions.

Many of these data will be a valuable asset for future young hepatologists in the Asia-Pacific region.



Dr. Arndt Vogel
Professor of Medicine, University of Toronto, Longo Family Chair in Liver Cancer Research Division of Gastroenterology and Hepatology, Toronto General Hospital Medical Oncology, Princess Margaret Cancer Centre Toronto General Hospital Research Institute, Schwartz Reisman Liver Research Centre Institute for Medical Science, Canada

Current Systemic Therapy in Liver Cancer: Present Achievements and Future Directions

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide currently experiencing a rising incidence, particularly in Western countries, driven by the increase in steatotic liver diseases. There is now a wide range of therapeutic options depending on the patient's performance status, liver function and tumor stage. These range from surgical procedures, such as liver transplantation and resection, to interventional therapies, such as ablation or transarterial chemoembolization, to systemic therapies in advanced stages. The recent approval of immunotherapies has significantly improved the landscape of systemic treatment options. Due to the diversity of therapeutic approaches, multidisciplinary care in experienced centers with a focus on liver tumors is crucial.

Systemic therapies are used in the advanced stage and in the intermediate stage if local therapies are not possible or there is no adequate response. In the meantime, multiple substances have been approved in this area, which have shown high efficacy with significantly improved overall survival. In this presentation, I will give an overview of the approved therapies and discuss the advantages and disadvantages of each therapy.

Dr. Changhoon Yoo
Department of Oncology, Asan Medical Center,
University of Ulsan College of Medicine,
South Korea

Advancing Systemic Therapy for Liver Cancer: Clinical Practice Insights and Research Initiatives to Meet Unmet Needs

Hepatocellular carcinoma (HCC) remains a significant global health challenge, particularly in advanced stages where systemic therapy becomes pivotal. The introduction of novel therapeutic agents has transformed the treatment paradigm for HCC, with the approval of multiple first-line therapies, including lenvatinib, atezolizumab plus bevacizumab (Atezo-Bev), durvalumab plus tremelimumab (STRIDE), and ipilimumab plus nivolumab (Ipi-Nivo).

Atezo-Bev has demonstrated a well-balanced efficacy profile in terms of overall response rates (ORR), progression-free survival (PFS), and overall survival (OS), with significant early clinical benefits. In contrast, STRIDE and Ipi-Nivo show robust long-term OS benefits despite inferior PFS and OS compared to Atezo-Bev. The safety profiles of these therapies must also be critically evaluated for treatment selection, considering adverse events (AEs) such as anti-angiogenesis-related AEs (including hypertension and proteinuria) and immune-related AEs. Atezo-Bev is noted for fewer steroid-requiring AEs, whereas STRIDE and Ipi-Nivo present higher incidences of immune-related toxicities. Clinical decision-making is complex and must account for patient-specific factors, including tumor burden, performance status, comorbidities, and patient preferences.

While the availability of more first-line therapy options with unique pros and cons in terms of efficacy and safety profiles complicates clinical decision-making, the absence of established biomarkers for predicting efficacy and toxicity further challenges treatment choices. Global collaboration is urgently needed to define biomarkers in unresectable HCC.

In conclusion, the rapid evolution of systemic therapies for HCC necessitates continuous evaluation of clinical data to refine treatment strategies. Future research should focus on optimizing combination regimens and exploring biomarkers to enhance patient selection and therapeutic outcomes.

Dr. Sadahisa Ogasawara
Department of Gastroenterology,
Graduate School of Medicine, Chiba University,
Japan

Harnessing the Power of Real-World Data to Address Clinical Challenges in Systemic Therapy for Advanced Hepatocellular Carcinoma

The 2020s have seen remarkable progress in systemic therapy for advanced hepatocellular carcinoma (HCC). To date, three combination immunotherapy regimens have demonstrated statistical significance in phase III trials. Two of these regimens (atezolizumab plus bevacizumab and durvalumab plus tremelimumab) have been established as standard first-line treatment in clinical practice. As a result, tyrosine kinase inhibitors (TKIs) with VEGF inhibitory activity and anti-VEGF-R2 antibodies, which were previously standard of care, are now being repositioned as second-line therapies after immunotherapy. Reviewing the history of drug development in advanced HCC, since 2007, when sorafenib demonstrated improved overall survival over placebo, almost all phase 3 trials have been designed with sorafenib as the standard first-line treatment. The exception is the recent CheckMate 9DW trial (nivolumab plus ipilimumab versus lenvatinib or sorafenib). In clinical practice, however, the availability of multiple agents, including regorafenib and lenvatinib, has led to different sequential treatment strategies. This has resulted in multiple treatment streams that were not anticipated in phase 3 trials. It is impractical to validate each of these approaches in individual prospective trials. While prospective interventional studies are critical to building evidence, it is challenging to address all clinical questions using this method alone. The use of real-world clinical data provides an opportunity to generate evidence in a more efficient and practical manner. This approach is gaining attention as a flexible and rapid means of generating evidence that is aligned with the rapidly evolving landscape of HCC treatment. The integration of data from both controlled clinical trials and real-world practice is becoming increasingly important. This combined approach allows for a more comprehensive understanding of treatment efficacy and safety in different patient populations and clinical scenarios. It also enables the identification of potential biomarkers and patient subgroups that may benefit from specific treatment strategies. As the field of HCC treatment continues to advance, the challenge is to balance the rigorous methodology of traditional clinical trials with the need for timely, real-world evidence. This hybrid approach to evidence generation is likely to play a critical role in shaping future treatment guidelines and personalized medicine strategies for patients with advanced HCC.

Dr. Masatoshi Kudo
Department of Gastroenterology and hepatology,
Kindai University Faculty of Medicine,
Japan

Pushing the Boundaries of Liver Cancer Treatment: Synergizing Locoregional Therapy and Immunotherapy

Even in non-inflamed tumors and tumors that are not suitable for TACE, administration of anti-VEGF agents/tyrosine kinase inhibitors (TKIs) can normalize blood vessels and enhance the effect of TACE. The combined effect of TACE and immune checkpoint inhibitors (ICIs) also results in volume reduction and cancer antigen release. An unfavorable effect is that TACE-induced hypoxia upregulates VEGF, which suppresses the activation of CD8-positive T cells and increases the number of immunosuppressive cells such as Tregs, MDSCs, and TAMs. However, continued administration of anti-VEGF agents suppresses the increase in VEGF. In addition, tumor cells that have been destroyed by TACE release cancer antigens and lead to the activation and maturation of dendritic cells (DCs). The CD8- positive T cells recognize the tumor antigen and become activated CD8, causing residual intratumor infiltration and killing the immune-evaded tumor cells through the effects of ICIs. Therefore, ICI plus anti-VEGF/TKI plus TACE is considerably more effective and synergistic than ICI plus anti-VEGF/TKI. Atezo/Bev plus TACE, Lenvatinib plus pembrolizumab in combination with TACE and Durvalumab plus bevacizumab in combination with TACE will change the treatment land scape of unresectable HCC.

Dr. Shinji Tanaka
Department of Molecular Oncology,
Tokyo Medical and Dental University,
Japan

Personalized Approaches to Liver Cancer Management: Molecular and Immunological Landscape to Develop Novel Strategies

The disease as “cancer” is established in vivo through the interactions between cancer cells and host-derived factors. Particularly in the liver, which is a parenchymal organ, it is essential to comprehensively understand the interactions within the unique microenvironment, host cell populations, and various chronic diseases that serve as a backdrop to these interactions. Recent advancements in genetic analysis technologies have led to the proposal of subtypes in hepatocellular carcinoma (HCC) based on Lee’s "two-class" model, including Boyault and Hoshida subclasses.

On the other hand, after the approval of the anti-angiogenic agent sorafenib for the treatment of HCC, a series of clinical trial failures ensued, leading to a decade-long period with no alternative treatment options. This period can be referred to as the "lost decade," during which the necessity of making treatment decisions based on prognostic predictions of the two-class model was not compelling. Subsequently, several anti-angiogenic agents and immune checkpoint inhibitors with combination therapies have been approved, significantly improving response rates to 20-30%. However, it has also been revealed that disease progression (PD) occurs at a similar rate. In this rapidly changing landscape, there is increasing attention on the significance of new molecular immunological subtype classifications that align with pathological histology, immune microenvironment, and clinical factors.

As treatments for hepatitis viruses have made remarkable progress, the tumor microenvironment against the backdrop of metabolic abnormalities has gained further attention. Clinical research is deepening the stratification of subtypes through single-cell and AI analyses, while preclinical research is actively developing new personalized therapies based on immunocompetent models that accurately replicate each subtype. Recently, the concept of the cancer-immunity cycle has been updated, emphasizing the continuous rotation (eddy) of the tumor microenvironment as a subcycle, and new therapeutic targets are being explored. It is crucial to consolidate the latest achievements in basic and clinical research on the tumor microenvironment in HCC.

Dr. Yosuke Togashi
Department of Tumor Microenvironment,
Faculty of Medicine, Dentistry and Pharmaceutical Sciences,
Okayama University
Japan

Tumor Microenvironment and Immune Response in Cancer

The effectiveness of cancer immunotherapies, including PD-1 blockade therapies, has been established; however, their efficacy is still inadequate, necessitating the development of reliable predictive biomarkers and more effective treatments. Key biomarkers such as PD-L1 expression, tumor-infiltrating lymphocytes (TILs), and somatic mutation burden are extensively studied, yet they do not allow for perfect prediction of outcomes. Given that PD-1 blockade therapies function by activating T cells, our research is specifically focused on TILs using real clinical specimens. TILs are notably heterogeneous, making it difficult to capture their true nature through bulk gene expression analysis, which only provides average values. We are advancing our understanding by performing detailed analyses at a single-cell level. Our approach involves analyzing patient-derived TILs through flow cytometry and/or single-cell sequencing. By challenging these TILs with corresponding patient-derived tumor cell lines, we have discovered that T-cell clones expressing high levels of exhaustion markers such as PD-1 and CD39 attack tumor cells directly and are critical for anti-tumor immune response. Detailed examination of these T-cell clones has enabled us to uncover specific abnormalities and identify therapeutic targets, leading to novel biomarkers and therapies.

Dr. Carmen Chak-Lui Wong
Associate Professor
Department of Pathology, State Key Laboratory of Liver Research,
LKS Faculty of Medicine, University of Hong Kong,
Hong Kong, China

Advancements and Future Directions in the Study of the Immune Landscape of Liver Cancer

Hepatocellular carcinoma (HCC) represents a serious global health burden, characterized by limited treatment options and a poor overall prognosis. The immune landscape of HCC is a critical factor influencing disease progression and therapeutic response. Currently, HCC patients are treated in a one-size-fits-all approach, with immune checkpoint inhibitors rising as the most common treatment. HCC exhibits high intertumoral heterogeneity caused by different combinations of mutations in multiple pathways. These tumors are biologically distinct and respond to treatments differently. Our team has established a library of murine HCC tumors through somatic genome-editing using the CRISPR-Cas9 and transposon systems, with genetic alterations resembling those found in human HCCs. This allows us to test their differential responses to immunotherapies. We performed single-cell RNA sequencing and high-dimensional analysis on the tumor-infiltrated immune cells (TILs) and found that specific genetic mutations (e.g., Keap1^{KO}Myc^{OE}) are associated with a high number of CD8+ T cell infiltrations, while other mutations (e.g., Tp53KOMycOE) are associated with a low number of CD8+ T cell infiltration. These tumors are referred to as hot and cold tumors, respectively. We discovered a significant distinction in the response to anti-PD-1 treatment between hot tumors, which exhibited positive responses, and cold tumors, which did not respond to anti-PD-1 monotherapy. Additionally, we studied TILs in cold tumors resistant to anti-PD-1 therapy using mass cytometry (CyTOF), enabling us to analyze close to 40 immune cell markers simultaneously. We found that anti-PD-1 resistant HCC must be treated with combination therapies such as anti-PD-1 + Sorafenib/lenvatinib and anti-PD-1 + anti-TIGIT. It is worth noting that human HCC often presents mutations in multiple pathways. Our highly adaptable mouse HCC model accurately replicates the alterations in specific pathways found in individual HCC patients, making it a promising tool for testing precision medicine. Gaining access to clinical specimens for certain clinical scenarios can be quite challenging, impeding our comprehension of the underlying molecular biology and pathogenesis. Therefore, this presentation will highlight the importance of somatic mouse models in bridging this knowledge gap. We will demonstrate how somatic mouse models can effectively be used to study steatotic/MASH-HCC and recurrent HCC, which are challenging to investigate due to the difficulty in obtaining specimens from these specific treatments. With the flexibility of somatic genome editing systems and the advent of cutting-edge technologies such as in vivo CRISPR-Cas9, mass cytometry, single-cell RNA sequencing, spatial transcriptomics, and cyclic imaging, we are currently in an unprecedented era of understanding the immune microenvironment. This presentation will illustrate how we can capitalize on these exciting tools to unravel the relationship between genomics and immunology in liver cancer in the era of precision medicine.

Dr. Takahiro Kodama
Department Gastroenterology and Hepatology,
Osaka University Graduate School of Medicine,
Japan

Challenging in Biomarker Discovery: Targeting the Tumor Microenvironment in Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) remains a severe disease, ranking third in cancer-related deaths. The treatment landscape for unresectable HCC has significantly evolved with the introduction of immunotherapy. Traditional treatments focused on multi-kinase inhibitors (MKIs) have given way to combined immunotherapy using immune checkpoint inhibitors (ICIs). Current guidelines recommend anti-PD-L1/anti-VEGF and anti-PD-L1/anti-CTLA-4 antibody combinations as first-line treatments, while MKIs like Lenvatinib and Sorafenib are now considered for second-line or later stages. However, only up to 30% of patients respond to these treatments, and immunotherapy can lead to severe immune-related adverse events (irAEs). The strategic use of these therapies is crucial for improving patient outcomes, yet no definitive biomarkers exist to guide optimal treatment choices.

This lecture will provide an overview of current research on predictive biomarkers for combination immunotherapy in uHCC. I will begin with a brief review of cancer immunity basics and the mechanisms of action of two key combination immunotherapies, focusing on the cancer immunity cycle. Next, I will discuss potential biomarkers for HCC immunotherapy. Common predictive factors in various cancers, such as PD-1/PD-L1 expression, TMB, and MSI-H, appear less effective for HCC. Conversely, factors derived from tumor microenvironment analyses, like intratumoral CD8+ T-cell infiltration and molecular signatures from gene expression profiling, have shown promise in predicting responses in HCC.

Additionally, our research explores liquid biopsy markers, including serum cytokines and circulating tumor DNA (ctDNA), along with clinical factors like neutrophil-lymphocyte ratio (NLR), prior antibiotic use, and MRI findings, as predictors of response and prognosis in combination immunotherapy. Lastly, I will touch on future directions in biomarker research for HCC combination immunotherapy.

Dr. Stephen Lam Chan
Department of Clinical Oncology,
The Chinese University of Hong Kong,
Hong Kong SAR, China

From Early to Advanced Stages: Navigating Hepatocellular Carcinoma Treatment with Systematic Therapy

Systemic therapy is conventionally administered to patients with advanced HCC. The recent rapid development on HCC has led to revolution of the concept in the management of HCC: 1) the role of TACE is further refined to patient with disease burden/condition who derive most benefits from the selective TACE. Patients with disease that are unsuitable for selective TACE are believed to derive benefit from the systemic therapy; 2) recent phase III clinical trial showed that the addition of immunotherapy and bevacizumab to TACE could improve the progression-free survival as compared to TACE alone. While more mature data are pending for this approach, this regimen will potentially benefit selected patients; 3) for early-stage HCC, there have been emerging clinical data on the use of adjuvant an neo-adjuvant immunotherapy for patients amenable to surgery or loco-ablation.

Dr. Yi-Hsiang Huang
Institute of Clinical Medicine, College of Medicine,
National Yang Ming Chiao Tung University,
Taiwan

Multifaceted Strategies for Hepatocellular Carcinoma in Asia: Improving Patient Outcomes with Optimal Treatment Modalities

Hepatocellular carcinoma (HCC) is characterized by heterogeneity in tumor burden and liver histology, especially in the unresectable state. There are multiple treatment options for unresectable HCC, including liver-directed therapies (TACE, TARE, SBRT) and systemic therapies or combination therapies. Tumor burden is a key factor associated with treatment response and survival to TACE. In out previous study, the 7-11 criteria may be more suitable for Asian countries to classify intermediate-stage HCC into low, intermediate, and high tumor burden. In patients with high tumor burden, TACE does not provide clinical benefit, so sequential or combined treatments should be considered. Radiologic pattern is another factor associated with tumor response to TACE. Our recent study confirms that confluent or infiltrative type HCC responds poorly to TACE and systemic therapy should be introduced for unfavorable radiologic features. To improve progression-free survival in intermediate-stage HCC, systemic therapy combined with TACE can be used in TACE-eligible cases based on Emerald-1 study. Lenvatinib combined with TACE also showed superiority in survival for intermediate to advanced HCC. For curative conversion of intermediate-stage HCC, liver-directed therapy, systemic therapy, or combined therapy followed by curative therapy may achieve a cancer-free and drug-free state. For immunotherapy of HCC, there is still a lack of clinically useful biomarkers to guide the selection of immunotherapy. Our recent study shows that gut microbiota and metabolites can potentially predict the progression-free survival and overall survival for patients with unresectable HCC undergoing immune checkpoint inhibitors (ICIs) therapy. In Asia, hepatitis B virus (HBV) infection remains a key driver of HCC development and recurrence. In order to improve the effect of HCC treatment, controlling HBV replication is also an important issue. Our recent studies demonstrate that HBV reactivation is rate during ICIs treatment if NUCs could be co-administered, and ICIs are potentially to achieve functional cure of HBV in patients with cancer and low HBsAg level. In summary, the survival rates for unresectable liver cancer can be improved though multi-modality approach and combination therapy.

Dr. Shinji Itoh
Department of Surgery and Science,
Graduate School of Medical Sciences, Kyushu University,
Japan

Surgical Resections in Hepatocellular Carcinoma: Evolving in Tandem with Advancements in Systemic Therapy

Surgical resections, including liver resection and liver transplantation, provide the most effective options for patients with hepatocellular carcinoma (HCC). 1) With advancements in technique, minimally invasive liver resection has gained widespread adoption worldwide due to its well-founded short-term benefits, with no compromise in oncologic outcomes compared to the traditional approach. Notably, robotic liver resection is being used more frequently, with supporters highlighting its enhanced dexterity due to wristed instruments, 3D visualization, integrated stapling, and a stable operating platform. 2) In Japan, since 2020, the national insurance scheme has permitted living-donor liver transplantation for patients with HCC who have Child-Pugh C cirrhosis, provided they meet the Japan criteria, which includes either the Milan criteria or the 5–5-500 rule. The adoption of the Japan criteria is significant in guiding the optimal treatment strategy for these patients, as it provides a clear framework for decision-making. Moreover, patients who undergo downstaging within the parameters set by the Japan criteria have shown favorable post-transplant outcomes. 3) With recent advancements in systemic therapy for HCC, there has been an increasing number of cases where multidisciplinary treatments are combined with surgery, including curative-intent conversion surgeries for patients with advanced HCC. In 2023, a consensus statement was issued by a panel of Japanese experts, outlining criteria for assessing the resectability of HCC from an oncological perspective. These criteria are classified as R (resectable), BR1 (borderline resectable 1), and BR2 (borderline resectable 2), and are based on the assumption that the tumors are technically and liver-functionally resectable. The development of these resectability criteria is significant as it aims to establish a standardized framework for discussing and evaluating treatment strategies for advanced HCC, providing a common language among clinicians and researchers. The criteria are expected to evolve, with further optimization, modifications, and updates anticipated as systemic therapies continue to advance and as additional validation studies are conducted. As the landscape of treatment options for advanced HCC expands, these resectability criteria will play a crucial role in guiding clinical decisions. They will also facilitate the categorization of patients based on their tumor status, distinguishing between those with technically unresectable tumors and those classified as BR1 or BR2 but technically resectable. This distinction is expected to encourage further clinical investigation into the role of surgery following systemic therapy in advanced HCC, potentially leading to improved outcomes for patients undergoing multidisciplinary treatment approaches.

Dr. Ryosuke Tateishi
Department of Gastroenterology,
The University of Tokyo Hospital,
Japan

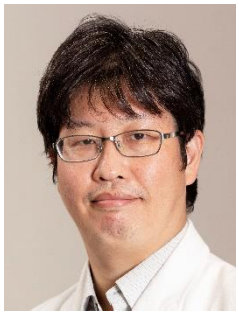
The Role of Percutaneous Ablation in the Treatment of Liver Cancer: A Response to Shifting Disease Patterns and Treatment Landscapes

Hepatocellular carcinoma (HCC) usually arises in chronic liver diseases, mainly viral hepatitis, and most of them are complicated by advanced liver fibrosis or cirrhosis. Consequently, the indication for hepatic resection is limited to approximately 30% to 40% of patients, and even if local radical resection is performed, recurrence occurs in 50% to 70% of patients within 5 years. Percutaneous ablation began with ethanol injection in 1983 as a treatment for patients with impaired liver function who could not undergo hepatic resection, and has evolved into first-generation microwave ablation (MWA), radiofrequency ablation, and second-generation MWA. In Japan, since most HCCs were caused by cirrhotic hepatitis C, surveillance mainly by abdominal ultrasound has been widely performed for these patients, and led to improvement in the prognosis of HCC patients through early diagnosis and repeated minimally invasive ablation. In recent years, the number of patients with active hepatitis C has decreased dramatically with the advent of direct-acting antiviral agents for hepatitis C and the natural decrease due to the aging population. On the other hand, lifestyle-related liver cancer, represented by metabolic dysfunction-associated fatty liver disease with obesity as a background, is increasing. As surveillance for non-viral HCC has not been established, patients are often diagnosed at an advanced stage in which ablation is not suitable. In addition, since percutaneous ablation is mainly performed under ultrasound guidance, there are some cases in which ablation is difficult to perform due to extreme obesity. On the other hand, the development of systemic therapy for advanced hepatocellular carcinoma has changed the role of ablation in the treatment of liver cancer. It has been reported that ablation of some nodules can improve the curative effect of systemic therapy, when treatment effect is considered insufficient. There are also reports of combination therapies to enhance the efficacy of immunotherapy, such as ablation to promote the release of tumor antigens. In conclusion minimally invasive and locally curative ablation therapy will continue to play an important role in the treatment of liver cancer.

Dr. Toshihiro Tanaka
Department of Diagnostic and Interventional Radiology,
Nara Medical University,
Japan

The Evolving Landscape of Transarterial Therapy for Liver Cancer: Current Practices and Emerging Trends

In the current systemic therapy era, the role of TACE has shifted from palliative treatment to curative treatment. Historically, achieving CR through TACE has been associated with prolonged overall survival of HCC patients including those in early stage. Notably, recent findings indicate that achieving CR also demonstrates a positive impact on patients with intermediate-stage HCC reported. In subclassifying intermediate-stage HCC, several criteria have been proposed, including Up-to-7 criteria, Up-to-11, 7-11, and Nr-11 criteria, which could be viable for determining the suitability of TACE. It is crucial to tailor treatment plans to the specific tumor burden and malignancy potential of each case. In recent years, imaging techniques and devices for TACE have been improved, making it possible to perform precise TACE procedure. Additionally, combination therapies with TACE and MTAs and/or ICIs are expected to improve therapeutic outcomes. In this presentation, I will introduce the current indications of TACE and key points of the TACE technique to achieve CR that we are implementing with the intention of standardization. We also discuss future perspectives on the combination therapies of TACE with systemic therapies.



Dr. Masaru Wakatsuki
QST Hospital,
National Institute for Quantum Science and Technology,
Japan

Radiation Therapy in Liver Cancer: Insights into Current Impact and Future Prospects

Radiofrequency ablation (RFA) and surgical resection are the first choices for curative treatment of early stage of hepatocellular carcinoma. However, we experience many cases in which these radical treatments are not indicated due to factors such as tumor localization, liver function, and complications. Stereotactic body radiation therapy (SBRT) and particle therapy are important options in such cases.

SBRT is becoming widely used as an effective treatment for relatively small hepatocellular carcinomas as an alternative to RFA and surgical resection. On the other hand, particle therapy such as carbon-ion beam therapy is a new radiation therapy that has been rapidly gaining popularity in recent years. Carbon-ion radiotherapy (C-ion RT) has improved dose distribution characteristics due to the Bragg peak and low transverse scattering, and can deliver a higher prescribed dose than photons to hepatocellular carcinoma. Taking advantage of these characteristics, C-ion RT is expected to be a new curative treatment method. The National Institutes for Quantum Science and Technology (former National Institute of Radiological Sciences) started treatment with C-ion RT in 1994, and has treated about 1,000 cases of hepatocellular carcinoma to date. Since then, the number of patients treated has been increasing. It has been shown to be a safe and effective treatment, especially for patients with hepatocellular carcinoma with vascular invasion, patients with impaired liver function, and patients with bulky hepatocellular carcinoma.

In this presentation, I would like to introduce the treatment for hepatocellular carcinoma with a focus on SBRT and C-ion RT, as well as the challenges and future direction of C-ion RT for hepatocellular carcinoma.

Memo

APASL Oncology 2024 Chiba

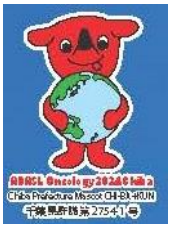
"Genomics Meets Immunology:
Interdisciplinary Approach for Liver Cancer"

Abstracts

Sponsored Seminars

Luncheon Seminars

Morning Seminars



Sponsored Seminar 1 (Sponsored by Eisai Co., Ltd.)

Dr. Junichi Shindoh
Department of Gastroenterological Surgery,
Toranomon Hospital,
Japan

Pushing the Envelope for Surgical Management of Advanced Hepatocellular Carcinoma

Recent introduction of effective systemic therapy has been changing the landscape of multidisciplinary treatment for hepatocellular carcinoma (HCC), while it remains unclear whether or not surgical intervention as a part of multidisciplinary treatment is truly beneficial for patients with advanced HCC. Since introduction of new biologic agents, increasing number of papers regarding the concept of "conversion surgery" have been published. However, lack of consensus on resectability of HCC has precluded constructive discussion on an optimal treatment strategy in the era of effective systemic therapy. In 2023, the working group between JLCA and JSHBPS launched new criteria for oncological resectability of HCC as the Expert Consensus Statement 2023, and several validation studies are currently on going. In this talk, updated clinical evidence and future perspective of multidisciplinary treatment for advanced HCC will be discussed from the standpoint of surgery.

Sponsored Seminar 2 (Sponsored by AbbVie G.K.)

Dr. Nobuharu Tamaki
Department of Gastroenterology and Hepatology,
Musashino Red Cross Hospital,
Japan

DAA Treatment for Chronic Hepatitis C and Future Challenges

Almost all patients with chronic hepatitis C could achieve sustained virological response (SVR) by direct acting antivirals (DAA) treatment. In a nationwide, prospective study including 1275 patients with chronic hepatitis C who received glecaprevir and pibrentasvir (GLE/PIB), the SVR rate was 99.1% (JGH Open, 2024 Apr 25;8(4):e13068.) High SVR were observed regardless of genotype or liver fibrosis status. Even in patients where liver fibrosis was underestimated and 8-week treatment was chosen, the SVR rate was 100%. GLE/PIB treatment is highly effective regardless of age or comorbidities and can therefore be used as a first-line treatment for the treatment of chronic hepatitis C(Hepatol Res. 2020 Jul;50(7):791-816.). There is still debate about appropriate follow-up after SVR. In Asian countries with a high proportion of elderly people, some patients have a high risk for hepatocellular carcinoma (HCC) even after SVR. Continued surveillance for HCC is necessary, especially in men over 60 years of age, as they have a higher risk of developing HCC after SVR. The presence of diabetes or steatotic liver disease is also a risk factor for HCC development. Because appropriate control of diabetes can reduce the risk of HCC, it is therefore important to control metabolic complications appropriately even after SVR. There are many cases of lean metabolic dysfunction-associated steatotic liver disease (MASLD) in Asia. Comparing lean MASLD with non-lean MASLD, the risk of liver-related complications was higher in lean MASLD. Therefore, the risk of HCC is high in lean MASLD and continued HCC surveillance is necessary in such cases.

Sponsored Seminar 3 (Sponsored by Chugai Pharmaceutical Co., Ltd.)

Dr. Teiji Kuzuya
Professor, Department of Gastroenterology and Hepatology,
Fujita Health University,
Japan

Real-World Clinical Impact of Atezolizumab plus Bevacizumab in Patients with Advanced Hepatocellular Carcinoma - A 4-Year Experience

It has been four years since the combination of atezolizumab and bevacizumab (Atz/Bev) became widely used in clinical practice for patients with advanced hepatocellular carcinoma (HCC).

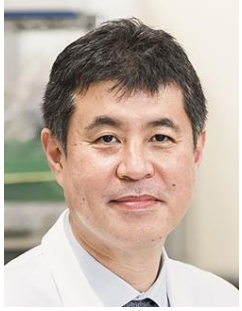
The ELIXIR study was a prospective, multicenter, observational study to determine the real-world clinical outcomes of Atz/Bev in Japanese patients. A total of 493 patients were enrolled, median age 73 years, 333 (67.5%) with Child-Pugh Score 5, 404 (81.9%) with PS 0 and 85 (17.2%) with VARIX 85 (17.2%, enrolled post-treatment if prophylaxis was required prior to treatment initiation). The rate of treatment-emergent adverse events was similar to that seen in the IMbrave150 trial: median progression-free survival (PFS) was 8.1 months, with no significant differences by age (75 years or older) or VARIX status. The results suggest that Atz/Bev is a highly effective and well-tolerated treatment in real-world clinical practice in a large elderly population.

The REPLACEMENT trial was a multicenter, single-arm, Phase II study designed to evaluate the efficacy and safety of Atz/Bev in TACE-ineligible patients with up to seven criteria for tumor burden in intermediate-stage HCC. 74 patients were enrolled with a median PFS of 9.1 months, the best anti-tumor response according to mRECIST. The objective response rate (ORR) and disease control rate (DCR) were 44.6% and 90.5%, respectively. A propensity score matching comparison of PFS between Atz/Bev and TACE (historical data) showed that the Atz/Bev group had significantly longer PFS at 7.4 months compared to 5.3 months in the TACE group (HR=0.59, p=0.042).

A multidisciplinary treatment strategy combining systemic therapy with local therapy is gaining attention with the goal of a cancer-free and drug-free patient. Kudo et al. conducted a multicenter, retrospective study to determine whether the addition of local therapy with curative intent is useful in increasing the rate of CR achieved in patients treated with Atz/Bev as primary therapy for unresectable and TACE-ineligible intermediate-stage HCC. Of 110 patients treated with Atz/Bev, 3 patients achieved CR with Atz/Bev alone and 35 patients were treated with radical therapy (liver resection in 7 patients, local puncture ablation in 13 patients, and radical TACE in 15 patients), resulting in overall CR (cancer-free) in 38 patients (35%), and 25 patients (23%) became drug free as a result of achieving CR.

In addition, the clinical outcomes of 139 patients treated with Atz/Bev at our institution will be presented, with a focus on the characteristics of patients who achieved CR and post-PD treatment strategies.

Sponsored Seminar 4 (Sponsored by Gilead Sciences K.K.)



Dr. Taro Yamashita
Department of Gastroenterology,
Kanazawa University School of Medicine,
Kanazawa University Hospital,
Japan

Prediction and Prevention of Hepatocellular Carcinoma in Chronic Liver Diseases

Chronic liver diseases associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) infection are major causes of hepatocellular carcinoma (HCC), the most prevalent primary liver malignancy and the third leading cause of cancer-related death worldwide. Therefore, regular surveillance for HCC is recommended in patients with chronic liver disease associated with HBV and HCV infection even after viral eradication, especially those with cirrhosis, to detect the tumors at an early stage when curative treatments are available. In addition to imaging studies, the use of biomarkers is also recommended for HCC surveillance in those patients. Several serum biomarkers, including alpha-fetoprotein (AFP), AFP-L3, and des-gamma-carboxy prothrombin (DCP), have been proposed as potential tools for the early detection of HCC.

Here, we introduce the laminin γ2 monomer (LG2m) as a potential biomarker for HCC surveillance in chronic viral hepatitis patients. In our previous multicenter prospective cohort study, we demonstrated the utility of serum LG2m measurement for predicting HCC in chronic hepatitis C patients who achieved sustained virological responses after treatment with direct-acting antivirals. Recently, we also observed the clinical utility of LG2m as a biomarker for HCC surveillance in patients with chronic HBV infection in a retrospective study. We also summarize the molecular mechanism of HCC development in the background of chronic liver diseases to develop a novel reagent for HCC prevention.

Sponsored Seminar 5 (Sponsored by FUJIFILM Wako Pure Chemical Corporation)

Dr. Hidenori Toyoda
Department of Gastroenterology,
Ogaki Municipal Hospital,
Japan

AFP-L3: An Old and New Marker Specific for the Management of HCC

AFP-L3 is a fraction of alpha-fetoprotein (AFP) that reacts *Lens culinaris* agglutinin. In previous studies, AFP-L3 has been reported as a tumor marker of hepatocellular carcinoma (HCC) that had high specificity. Other two tumor markers of HCC, i.e., AFP and des-gamma-carboxy prothrombin (DCP), often show the elevation or fluctuation in the absence of HCC. For example, AFP elevates in association with liver injury and DCP elevates in association with malnutrition. In contrast, AFP-L3 elevates specifically in association with the development of HCC.

AFP-L3 is reportedly associated with the aggressive nature of HCC tumor, and the elevation of AFP-L3 indicates poor prognosis with shorter overall survivals (OS) of patients. Previous pathological study reported that HCC with AFP-L3 elevation showed high rates of infiltrative growth, capsule infiltration, microscopic portal vein invasion and hepatic vein invasion, and moderate/poor differentiation, which may contribute to the shorter OS of patients. In addition, the combination of three tumor markers of HCC, i.e., AFP, AFP-L3, and DCP, along with liver function, well stratified OS in the entire HCC patients and patients with advanced unresectable HCC who underwent current systemic therapies.

In addition to the role of AFP-L3 as a diagnostic marker of HCC with high specificity and as a predictor of poor prognosis, recent studies revealed the significance of AFP-L3 in the surveillance of HCC, especially in the era of non-viral HCC. The significance of AFP as a surveillance marker is being reduced in patients with cured HCV infection or those with metabolic dysfunction-associated steatotic liver disease. In this context, the usefulness of AFP-L3 as a supplementary marker of AFP for HCC surveillance will be increasing as well as DCP. HCC is sometimes detected by the elevation with AFP-L3 solely as a trigger of cross-sectional studies, whereas AFP remained within normal range with minute fluctuation. In particular, the combination of AFP, AFP-L3, and DCP is expected to enhance the ability for indicating the development of the HCC.

Luncheon Seminar 1 (Sponsored by Gilead Sciences K.K.)

Dr. Toshifumi Tada
Division of Gastroenterology,
Department of Internal Medicine,
Kobe University Graduate School of Medicine,
Japan

Hepatitis C Treatment Progress Towards Elimination and Post-SVR Issues

Hepatitis C virus (HCV), discovered in 1989, remains a significant cause of hepatocellular carcinoma (HCC) in Japan a quarter-century later. It is well-established that HCC risk escalates with HCV-induced liver fibrosis progression. Our Markov model-based study simulated HCC development, starting from chronic hepatitis or cirrhosis at age 60, showing prevalent cases among both genders beyond 80 years old in untreated HCV scenarios. Additionally, HCV correlates not only with liver ailments but also with lymphoma, type 2 diabetes, and cardiovascular diseases. Analyzing 618 patients under interferon-based therapy, with and without sustained virologic response (SVR), we found SVR significantly lowered liver disease-related deaths (HR 0.149) and deaths due to non-liver causes (HR 0.439), suggesting potential mortality reductions across various systemic illnesses following HCV elimination. Similar risk reductions were observed with direct-acting antivirals (DAAs) for both liver and non-liver disease-related deaths. Concerning development of HCC by post-DAA-induced SVR, our study introduced the ADRES (after direct-acting antivirals recommendation for surveillance) score, integrating gender, AFP, and FIB-4 index. We observed significantly reduced HRs for HCC development across ADRES score categories (0 to 1/2/3: 2.947/9.171/20.630), enabling risk stratification. Additionally, the role of liver stiffness in predicting carcinogenesis and the necessity of hepatologist-led HCC surveillance post-SVR were emphasized. This presentation will highlight the transformative potential of SVR to reduce both HCV-related liver disease and systemic disease-related mortality, and outline the need for continued vigilance and specialized care in post-treatment management.

Luncheon Seminar 1 (Sponsored by Gilead Sciences K.K.)

Dr. Motoyuki Otsuka
Department of Gastroenterology and Hepatology,
Academic Field of Medicine, Density and Pharmaceutical Sciences,
Okayama University,
Japan

Innovative Strategies for Treating HBV-Related HCC: Insights from Basic Research

We are conducting research aiming at the complete eradication of HBV. During such research, we realized that the insights gained in this process can also be applied to the treatment of HBV-related liver cancer. For example, HBV promotes viral replication through the action of the HBx protein, which degrades the Smc5/6 protein complex. This degradation of the Smc5/6 protein complexes can weaken the genome repair mechanisms, potentially leading to liver carcinogenesis. In such cancers, it has been confirmed that complete inhibition of the genome repair mechanism by PARP inhibitors can lead to the “synthetic lethality”, effectively killing cancer cells more efficiently.
Furthermore, cabozantinib may be more effective against liver cancer associated with hepatitis B. This is suggested to be due to its ability to inhibit the activation of STAT3, making it more effective against liver cancer resulting from the integration of the HBV genome.
We believe that treatment selection based on the molecular pathology of liver cancer or based on the etiology could become one of the factors required for consideration when selecting liver cancer treatment methods.

Dr. Takeshi Terashima
Associate Professor,
Advanced Preventive Medical Sciences Research Center,
Kanazawa University,
Japan

Remaining Clinical Questions and Unmet Needs in the Era of Immunotherapy for Unresectable Hepatocellular Carcinoma

In recent years, two immunotherapy regimens consisting of atezolizumab and bevacizumab (Atezo+Bev) or durvalumab and tremelimumab have been shown to be useful, and have currently been established as the standard of care for advanced hepatocellular carcinoma (HCC). In addition, the CheckMate 9DW has verified the efficacy of nivolumab plus ipilimumab combination therapy.
A global phase III trial, IMbrave150, to verify the efficacy and safety Atezo+Bev combination therapy compared to sorafenib, included the patients with unresectable HCC and good liver functional reserve without prior systemic treatment. Under clinical practice, the patients excluded form the clinical trial may be candidates for treatment. However, the efficacy and safety of the combination therapy in patients with Child-Pugh classification B, previously treated with systemic therapy, or taking anticoagulants remains unclear and need to be confirmed by prospective studies. Another concern is the safety of long-term administration of high-dose bevacizumab. Proteinuria or impaired hepatic reserve not only reduce the therapeutic intensity of this combination therapy, but also adversely affect the introduction of posttreatment and the patient's quality of life.
Challenges to improve therapeutic efficacy continue. Some local treatments have been suggested to increase the efficacy of immunotherapy, and subsequent treatment also remains important to prolong overall survival by prolonging post-progression survival.
I will introduce the clinical trial results and our experience under clinical practice of Atezo+Bev combination therapy, and hope to have an opportunity for discussing some issues for patients with unresectable HCC.

Dr. Shohei Komatsu
Associate Professor,
Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery,
Kobe University Graduate School of Medicine,
Japan

Future Perspectives of Systemic Chemotherapy and Surgery in the Treatment of Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the most prevalent primary liver cancer and is one of the leading causes of cancer-related deaths worldwide. Since HCC is rarely detected at an early stage, only a small number of patients are eligible for curative treatments, including hepatectomy, radiofrequency ablation, and liver transplantation. The majority of patients are diagnosed with more advanced stage, and systemic chemotherapy is generally the recommended treatment option.

Along with the recent development of novel chemotherapeutic options, the treatment algorithm of HCC changed dramatically over time. The therapeutic range of systemic chemotherapy for “unresectable” HCC is steadily expanding. However, the definitions of “resectable or unresectable” varies among physicians or institutions. Because the indication of hepatectomy for HCC must be considered based on the oncological, liver functional, and technical factors, consensus has not yet been reached. Recently, the oncological resectability criteria for HCC have been established (R/BR1/BR2) by expert consensus meeting in 2023. The concept of unresectable is not established, and borderline resectable is classified into two categories (BR1/BR2). This is a groundbreaking concept that could be discussed with a uniform criterion at least on oncological issues. The evaluation of treatment outcomes with hepatectomy and systemic chemotherapy based on the oncological resectability criteria will be necessary to discuss the future perspectives of multidisciplinary treatment of HCC.

Based on the favorable objective responses of lenvatinib, atezolizumab plus bevacizumab, and durvalumab plus tremelimumab, a concept of conversion therapy, combining systemic chemotherapy and sequential local treatments, has attracted considerable attention in recent years. While the concept of “conversion” has also not yet been unified, there is a growing number of reports regarding the combination therapy with systemic chemotherapy followed by sequential local treatments.

This paper will discuss treatment outcomes based on the oncological resectability criteria and current status of conversion therapy with examples from our own experience and literature review.

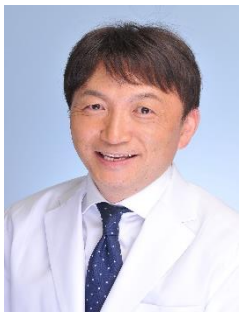
Luncheon Seminar 3 (Sponsored by AbbVie G.K.)

Dr. Yasuteru Kondo
Department of Hepatology,
Sendai Tokushukai Hospital,
Japan

Multidisciplinary Treatment Including Ultra-FP, iCIs and Ablation Therapy should be Considered to Control HCC

Recently, Dual iCIs and iCIs with VEGF-Ab could be used for the treatment of advanced stage HCC in Japan. However, Alternative treatment modalities are necessary because of the low response rates and unsuitability of molecular-targeted agents (MTA) and/or immune checkpoint inhibitors (iCIs) in HCC patients. The transarterial chemoembolization (TACE) and hepatic artery infusion chemotherapy (HAIC) have been improved by various kinds of methods. The liver resection, radiofrequency ablation (RFA) and microwave coagulation (MWA) could achieve complete response. However, the treatment indication of liver resection, RFA and MWA should be limited. Therefore, multidisciplinary treatment including HAIC, TACE, MTA, iCIs, RFA, MWA, and liver resection should be considered to control HCC. In this lecture, I will present about the role of Ultra-FP therapy (DEB-TACE and HAIC) and iCls for the HCC patients. Moreover, I will present about the role of ablation therapy after the achievement of HCC volume reduction.

Luncheon Seminar 3 (Sponsored by AbbVie G.K.)



Dr. Hironao Okubo
Department of Gastroenterology,
Juntendo University Nerima Hospital,
Japan

Pharmacokinetics of Direct-Acting Antiviral Therapy for Hepatitis C Virus Infection

Direct-acting antiviral (DAA) therapy for hepatitis C virus (HCV) infection has demonstrated a sustained virologic response rate of approximately 100%, leading to the recommendation for the treatment of most HCV-positive patients. Considering the current status, the safe use of DAA is growing in significance. Various factors, such as hepatic impairment, renal impairment, genetic polymorphisms, and drug interactions, can elevate the blood concentrations of DAAs and concomitant drugs. In particular, the pharmacokinetics of DAAs in patients with impaired hepatic function is significantly influenced by reduced cytochrome P450 activity, portal hypertension, diminished drug uptake into hepatocytes, and diminished drug protein binding due to hypoalbuminemia. Therefore, it is crucial to understand the pharmacokinetic properties of each DAA and factors that may alter the pharmacokinetics of each DAA. Glecaprevir, a NS3/4A protease inhibitor, is a substrate and inhibitor for organic anion transporting-polypeptide (OATP) 1B1 and 1B3, which are hepatic uptake transporters. Therefore, it is crucial to exercise caution when evaluating potential drug interactions with statins. Furthermore, the development of hyperbilirubinemia resulting from drug-bilirubin interactions is often observed in patients receiving glecaprevir/pibrentasvir therapy, and there is currently a lack of effective methods for predicting hyperbilirubinemia. In this lecture, we provide a comprehensive review of HCV DAA therapy with a focus on pharmacokinetics and discuss methods to predict drug adverse reactions.

Luncheon Seminar 4 (Sponsored by Eisai Co., Ltd.)

Dr. Naoto Fujiwara
Department of Gastroenterology and Hepatology,
Graduate School of Medicine,
Mie University,
Japan

Hepatocellular Carcinoma Treatment in the Era of Combined Immunotherapy -Future Role of Lenvatinib in Light of the Tumor Immune Microenvironment-

In the rapidly evolving field of hepatocellular carcinoma (HCC) treatment, the paradigm is shifting towards a more integrated approach that combines targeted therapies with immunotherapies. Among these, lenvatinib, a potent multitargeted tyrosine kinase inhibitor, has attracted significant attention because of its dual ability to directly inhibit tumor growth and potentially modulate the immune microenvironment. Our previous multi-omics analyses of surgically resected HCC tissues after lenvatinib treatment suggested that lenvatinib may transform the immune milieu from an immunosuppressive to a relatively immunoreactive state. This modulation is mainly characterized by significantly reduced VEGF signaling and subsequent normalization of aberrant VEGF-mediated permeability and hypoxia, resulting in increased infiltration of cytotoxic Granzyme K+ CD8 T cells through upregulation of chemotactic *CXCL9* in tumor-associated macrophages. Other clinical and experimental studies have also demonstrated the immunomodulatory effects of lenvatinib in HCC and other malignancies. This presentation focuses on the strategic role of lenvatinib within the framework of combined immunotherapy and revisits the therapeutic sequence for HCC from a molecular perspective with recent scientific evidence. By understanding the molecular mechanisms underlying its effects, we can optimize its use in combination therapies, ultimately improving the outcome of patients with HCC.

Luncheon Seminar 4 (Sponsored by Eisai Co., Ltd.)

Dr. Issei Saeki
Department of Gastroenterology and Hepatology,
Yamaguchi University Graduate School of Medicine,
Japan

Lenvatinib-based Treatment Strategy for Unresectable Hepatocellular Carcinoma

In recent decades, the prognosis of hepatocellular carcinoma (HCC) has been prolonged with various systemic therapies. In particular, there has been a remarkable improvement in the prognosis of patients with intermediate to advanced stage HCC, and the advent of systemic agent with high response rates, such as lenvatinib or combined immunotherapy, has been a breakthrough. Until now, the treatment strategy has been a simple one-to-one strategy; curative therapy such as resection and ablation for early-stage HCC, transarterial therapy for intermediate-stage HCC, and systemic therapy for advanced-stag HCC. However, it is now reported that transarterial therapy is not suitable for some patients with intermediate-stage HCC. In such cases, systemic therapy or TACE in combination with systemic therapy may be useful. Recently, we have experienced cases in which downstaging was achieved following systemic therapy with a high response rate, and leading to curative treatment. Currently, systemic intervention with TACE, such as hypoxia or tumor antigen release in mind is attracting attention, and a number of clinical trials are on-going to verify the usefulness of TACE in combination with systemic therapy. Furthermore, last year the JSHBPS and JLCA proposed the Oncological Criteria of Resectability for Hepatocellular Carcinoma. Until then, each institution has discussed surgical outcomes and pre- and postoperative treatment using own resectability criteria. Now this expert consensus established a common classification of preoperative tumor status. Various neoadjuvant and adjuvant therapies including immunotherapy, have been designed, and strategies for perioperative therapy are expected to be developed.

In this seminar, we will review the TACTICS trials, which are the milestones of TACE combined with systemic therapy performed in Japan. In addition, we will discuss future strategies for the treatment of intermediate to advanced HCC, highlighting the cases in our institution.

Dr. Makoto Ueno
Director, Department of Gastroenterology, Kanagawa Cancer Center,
Kanagawa Prefectural Hospital,
Japan

New Treatment Strategy for Intrahepatic Cholangiocarcinoma

Intrahepatic cholangiocarcinoma(iCCA) is the 2nd most common type of primary liver cancer, and its proportion of iCCA among primary liver cancers is increasing year by year. iCCA has different genetic properties and treatment prognosis from hepatocellular carcinoma and other biliary tract cancers(BTC). And it is necessary to consider an independent treatment strategy for iCCA. The JLCA has published the iCCA Clinical Practice Guidelines in 2021. As drug therapies for unresectable BTC, gemcitabine (G) + cisplatin (C) + S1 (S) combination, GC combination and GS combination have been recommended as standard cares in 1L, but based upon the results of the TOPAZ-1 trial, the 1st immune checkpoint inhibitor (ICI), durvalumab was approved in 2022. In addition, Pembrolizumab in combination with GC was also approved in 2024. Currently two ICIs are being used under medical insurance.

In Japan, NGS test which is cancer gene panel (CGP) testing was approved in 2019, and the number of tests performed in Japan has been increasing year by year. Regarding the number of tests by cancer type, BTC is the 3rd most frequently tested cancer in Japan. The background to this is that it is known that the expression profile of driver genes differs depending on the site of onset in BTC, and in particular, iCCA is known to be an area rich in druggable genes, MSI-High or TMB-High, *NTRK* fusion genes, *FGFR*2 fusion genes, and *BRAF* mutations. The frequency of FGFR2 fusion genes in iCCA has been reported to be 5.3% to 13.6% in Japan. Pemigatinib(PEM), an FGFR inhibitor, was launched in June 2021 and has been used in more than 130 cases in Japan so far. Recently, real-world data on PEM has been reported in Europe & US. It is critical to keep in mind that it takes about 6 weeks for the CGP test to be completed after obtaining consent from the patient, and to collect a sufficient amount of sample for the test from the time of diagnosis and to submit the patient for testing as early as possible. In the presentation, the results on the CGP test in Kanagawa Cancer Center (incl liquid test) will be shown. In the future, molecular targeted drugs targeting *HER*2, *MDM*2, etc. may appear, and in the field of iCCA, personalized treatment based on CGP testing is expected to become the standard for second-line treatment, and further improvement in prognosis is expected.

Dr. Hiroshi Ohno
RIKEN Center for Integrative Medical Sciences,
Japan

Gut Microbiota in Host Health and Diseases Including Gastrointestinal Cancers

Gastrointestinal tracts of animals including humans host numerous bacteria, collectively called gut microbiota. In the human colon, it is estimated to reach more than 40 trillions, which exceed the number of somatic cells constituting our body. There are hundreds of different bacterial species in individual human gut microbiota, with hundred thousands to a million of genes in total in each individual. Recent advances in gut microbiota studies have revealed that gut microbiota profoundly impacts the host health and diseases.

To understand the molecular mechanisms of host-gut microbiota interaction, we have been applying the integrated omics approach, where different layers of exhausted omics analyses such as (meta)genomics, epigenomics, transcriptomics and metabolomics, are combined. We have reported that a major metabolites of gut microbiota, short-chain fatty acids, namely acetate, propionate and butyrate, are involved in regulation of the host defense and immune responses in the gut. We have also reported that gut microbiota modulates the pathogenesis of autoimmune diseases such as type 1 diabetes and multiple sclerosis, allergic diseases as well as metabolic disorders such as obesity and type 2 diabetes.

I also discuss about the gut microbiota and cancers in digestive organs including the liver and pancreas.

APASL Oncology 2024 Chiba

"Genomics Meets Immunology:

Interdisciplinary Approach for Liver Cancer"

Abstracts

Plenary Session

O-1
10041

Long-term Hepatocellular Carcinoma Occurrence Rate after Administration of Nucleos(t)ide Analogues in Patients with Persistent HBV Infection

Kazuhiro Murai[1], Hayato Hikita[1], Ryoko Yamada[1], Yuki Tahata[1], Hisashi Ishida[2], Atsushi Hosui[3], Masanori Miyazaki[4], Ryotaro Sakamori[5], Nobuyuki Tatsumi[6], Kazuyoshi Ohkawa[7], Yoshinori Doi[8], Takatoshi Nawa[9], Satoshi Egawa[10], Yuichi Yoshida[11], Yasutoshi Nozaki[12], Kazuho Imanaka[13], Yoshinobu Saito[1], Takahiro Kodama[1], Tomohide Tatsumi[1], Tetsuo Takehara[1]

[1]Department of Gastroenterology and Hepatology, Osaka University, Graduate School of Medicine, Osaka, [2]Department of Gastroenterology and Hepatology, Ikeda Municipal Hospital, Osaka, [3]Department of Gastroenterology and Hepatology, Osaka Rosai Hospital, Osaka, [4]Department of Gastroenterology and Hepatology, Osaka Police Hospital, Osaka, [5]Department of Gastroenterology and Hepatology, NHO Osaka National Hospital, Osaka, [6]Department of Gastroenterology and Hepatology, Japan Community Healthcare Organization Osaka Hospital, Osaka, [7]Department of Hepatobiliary and Pancreatic Oncology, Osaka International Cancer Institute, Osaka, Japan, [8]Department of Gastroenterology and Hepatology, Otemae Hospital, Osaka, [9]Department of Gastroenterology and Hepatology, Higashiosaka City Medical Center, Osaka, [10]Department of Gastroenterology and Hepatology, Kinki Central Hospital of Mutual Aid Association of Public School Teachers, Hyogo, [11]Department of Gastroenterology and Hepatology, Suita Municipal Hospital, Osaka, [12]Department of Gastroenterology and Hepatology, Kansai Rosai Hospital, Hyogo,[13]Department of Gastroenterology and Hepatology, Itami City Hospital, Hyogo, Japan

Background and Aim: Nucleos(t)ide analogues (NUCs) are used for chronic hepatitis B (CHB) treatment. The effect of prolonged NUC administration on hepatocellular carcinoma (HCC) development remains unclear. This study investigates the suppressive effect of prolonged NUC administration on HCC in CHB patients.
Methods: This multicenter, observational study enrolled patients who received their first NUC dose between July 2000 and March 2019. We excluded patients with history of HCC or HCC occurrence within 1 year after NUC initiation.
Results: Among 703 CHB patients (143 with cirrhosis) initiating NUC treatment, 110 developed HCC during a median observation period of 106.2 months. The cumulative HCC incidence after NUC therapy was 5.6% at 3 years, 9.5% at 5 years, and 13.6% at 7 years. COX proportional hazards model revelated that presence of cirrhosis, older age, and high γ-GTP level at the time of NUC initiation were independent risk factors for HCC occurrence. Cumulative HCC incidence rate is significantly higher in cirrhotic patients than non-cirrhotic patients (20.6% vs 1.7% at 3 years, 33.1% vs 3.2% at 5 years, and 39.8% vs 6.6% at 7 years, $p<0.0001$ by log rank test). The annual HCC incidence rate was lower after 5 years than within 5 years of NUC initiation in cirrhotic patients, while remained similar 5 years after NUC initiation in non-cirrhotic patients.Landmark analysis at 5 years post-NUC initiation revealed still higher cumulative HCC incidence in cirrhotic patients than non-cirrhotic patients ($p<0.0001$ by log rank test).
Conclusion: HCC occurrence rate persists long-term after NUC administration.

O-2
10016

Spatial Omics Analysis of the Proximity of PD-L1(+) Tumor-Associated Macrophage and CD8T cell Interaction Promoting Hepatocellular Carcinoma Progression

Takuto Nosaka, Masahiro Ohtani, Junki Yamashita, Yosuke Murata, Tomoko Tanaka, Yu Akazawa, Kazuto Takahashi, Tatsushi Naito, Yasunari Nakamoto

Second Department of Internal Medicine, University of Fukui, Japan

Background: Spatial omics enables visualization of the tumor immune microenvironment and analysis of immune cell interactions. We examine proximity of PD-L1(+)TAMs and immune cells, based on spatial location and association with prognosis of hepatocellular carcinoma (HCC) using multiplex-immunohistochemistry (mIHC). Further, we investigate factors related to interaction of immune cells and mechanism of cancer progression.
Methods: mIHC (CD8, CD68, CD163, CD11c, PD-L1, DAPI) was performed on 90 resected HCC specimens. Cell distribution in the tumor center/tumor border/non-tumor border/non-tumor area were determined using inForm. Intercellular distances and the interaction variable (proportion of target cells within 25μm) was calculated. The mouse HCC cell line, BNL, transfected with GM-CSF vector was intraportally injected into Balb/c mice. αGM-CSF and/or αPD-L1 antibody were injected.
Results: In the tumor center, higher interaction variable of PD-L1(+)TAMs and CD8T cells had significantly worse in recurrence and survival rates. The interaction variable positively correlated with the number of GM-CSF(+)cells which were expressed by PanCK(+)tumor cells. In a mouse model, GM-CSF-transfected BNL cells increased tumor size and the interaction variable and decreased the number of GZMB(+)CD8T cells. αGM-CSF Ab reduced tumor size and the combination with αPD-L1 Ab further reduced tumor size. In qRT-PCR, αGM-CSF Ab decreased PD-L1 in TAM, and decreased PD1 and increased GZMB expression in CD8T.**Conclusion:** Spatial analysis revealed correlation of proximity between PD-L1(+)TAMs and CD8T with overall survival. Tumor cell-derived GM-CSF correlated with the proximity and promote PD-L1 expression in TAMs and CD8T exhaustion. GM-CSF and PD-L1 serve as new therapeutic targets to regulate tumor progression.

O-3
10064

Comparative Pathological and Comprehensive Genomic Analysis for Differential Diagnosis between IM and MC

Kenji Amemiya[1], Yosuke Hirotsu[1], Yusuke Kouchi[2,3], Ryosuke Tajiri[3], Yuji Iimuro[4], Masao Omata[1,5]
[1]Genome Analysis Center, Yamanashi Central Hospital. Yamanashi, Japan, [2]Department of Pathology, Chiba University Hospital, Chiba, Japan, [3]Department of Pathology, Yamanashi Central Hospital. Yamanashi, Japan, [4]Department of Surgery, Yamanashi Central Hospital, Yamanashi, Japan, [5]he University of Tokyo, Tokyo, Japan

Background: Accurate differentiation between intrahepatic metastasis (IM) and multicentric carcinogenesis (MC) in multifocal hepatocellular carcinoma (HCC) is crucial for guiding clinical management. This study aimed to compare the efficacy of pathological and comprehensive genomic analyses in differentiating IM from MC.
Methods: This study included 68 patients with multifocal HCC, encompassing 193 tumor lesions (82 synchronous, 111 metachronous). Genomic profiling of 72 HCC-related genes (59016 aa) was performed using next-generation sequencing.
Results: A total of 252 and 445 somatic mutations were identified in synchronous and metachronous tumors, respectively. Synchronous tumors exhibited an average of 3.1 somatic mutations and 0.7 oncogenic mutations per lesion. Metachronous tumors demonstrated 4.0 somatic mutations and 1.0 oncogenic mutations per lesion. Pathological diagnosis categorized synchronous tumors as IM:MC:IM&MC = 1:31:1. However, comprehensive genomic analyses reclassified these tumors as IM:MC:IM&MC = 8:24:1. Based on genomic diagnosis, the accuracy of pathological diagnosis for IM, MC and IM&MC was 1/8 (12.5%), 24/24 (100%) and 1/1 (100%).
Conclusion: Pathological diagnosis alone was insufficient to accurately differentiate IM from MC in multifocal HCC. Comprehensive genomic analysis demonstrated superior diagnostic accuracy and should be considered an integral component in the evaluation of multifocal HCC. We plan to report the results, including those on metachronous tumors, in the presentation.

O-4
10118

Relationship between Anti-tumor Response and Immune-mediated Adverse Events Requiring High-dose Corticosteroids in Unresectable Hepatocellular Carcinoma Treated with Durvalumab plus Tremelimumab

Takanori Ito[1,10], Shigeo Shimose[2,10], Joji Tani[3,10], Tetsu Tomonari[4,10], Issei Saeki[5,10], Yasuto Takeuchi[6,10], Takeshi Hatanaka[7,10], Kyo Sasaki[8,10], Soji Nishina[8], Motoyuki Otsuka[9], Taro Takami[5], Tetsuji Takayama[4], Takumi Kawaguchi[2], Hiroki Kawashima[1]
[1]Department of Gastroenterology and Hepatology, Nagoya University Hospital, Nagoya, [2]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, [3]Department of Gastroenterology and Neurology, Kagawa University, Faculty of Medicine, Kagawa, [4]Department of Gastroenterology and Oncology, Institute of Biomedical Sciences, Tokushima University Graduate School of Medicine, Tokushima, [5]Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Yamaguchi, [6]Department of Regenerative Medicine, Center for Innovative Clinical Medicine, Okayama University Hospital, Okayama, Japan, [7]Department of Gastroenterology, Gunma Saiseikai Maebashi Hospital, Maebashi, [8]Department of Gastroenterology, Kawasaki Medical School, Okayama, [9]Department of Gastroenterology and Hepatology, Okayama University Hospital, Okayama, [10]Hepatology InVestigator Experts in Japan (HIVE-J) Study Group

Background: Durvalumab plus tremelimumab (Dur/Tre) is an option as a first-line systemic treatment for patients with unresectable hepatocellular carcinoma (u-HCC). However, the management of severe cases with immune-mediated adverse events (imAEs) is a clinical problem. Thus, we investigated the relationship between severe imAEs and anti-tumor response in uHCC patients treated with Dur/Tre.
Methods: One hundred fifty-seven uHCC patients treated with Dur/Tre in a multicenter study group were included. We retrospectively analyzed the relationship between progression-free survival (PFS)/anti-tumor response and imAEs requiring high-dose corticosteroids.
Results: During a median observation period of 6.8 months, 32 patients (20.4%) developed severe imAEs. The types of these imAEs were as follows: enterocolitis (n=10), hepatotoxicity (n=9), lung injury (n=5), rash (n=4), fever/CRS (n=2), pancreatitis (n=2), and others (n=4). Infliximab was administered in 6 cases of enterocolitis. By treatment line, there was no significant difference in severe imAEs frequency (P=0.221). The ORR and DCR were 15.6/17.6% and 65.6/47.2%, respectively, for patients with and without severe imAEs, with no significant difference. On the other hand, in the patients who achieved an objective response (PR/CR), PFS at 10 months was 100% and 70.3% with and without high-dose corticosteroids, respectively, indicating that good PFS was achieved. Five patients with severe imAEs, including rash and hepatotoxicity, showed an objective response, while the incidence of enterocolitis was not associated with an objective response.
Conclusions: Severe imAEs requiring high-dose corticosteroids in Dur/Tre treatment did not increase antitumor efficacy, but it is important to manage imAE to lead to sequential therapy appropriately.

O-5
10154

Prognostic Factors after Carbon-ion Radiotherapy: A Study Based on Multi-institutional Registry Data

Kei Shibuya[1], Masaru Wakatsuki[2], Kazuki Terashima[3], Shingo Toyama[4], Hiroyuki Katoh[5], Osamu Suzuki[6], Hiroshi Tsuji[2], Tatsuya Ohno[1]
[1]Department of Radiation Oncology/Heavy-ion Medical Center, Gunma University Hospital, Maebashi, [2]QST Hospital, National Institutes for Quantum Science and Technology, [3]Department of Radiology, Hyogo Ion Beam Medical Center, [4]Ion Beam Therapy Center, SAGA-HIMAT Foundation, [5]Department of Radiation Oncology, Kanagawa Cancer Center, [6]Osaka Heavy Ion Therapy Center, Japan

Background: Carbon-ion radiotherapy (CIRT) is an emerging treatment for hepatocellular carcinoma (HCC). This study aimed to identify prognostic factors for CIRT outcomes in HCC patients using data from the Japan carbon-ion radiation oncology study group (J-CROS) nationwide multicenter registry.
Methods: We analyzed 260 HCC cases treated with CIRT between May 2016 and June 2018. Treatment protocols varied based on tumor location, with doses ranging from 48.0-76.0Gy (RBE) in 2-20 fractions. Multivariate analysis was performed to identify factors influencing overall survival (OS), progression-free survival (PFS), and local control (LC).
Results: With a median follow-up of 35.5 months, the 3-year OS, PFS, and LC rates were 85.7%, 43.7%, and 66.3%, respectively. Multivariate analysis revealed that elevated AFP levels (>50 ng/mL) were a significant poor prognostic factor for OS (HR 2.65, 95% CI 1.21-5.83, p=0.02), PFS (HR 2.19, 95% CI 1.54-3.11, p<0.01), and LC (HR 1.83, 95% CI 1.13-2.98, p=0.02). Tumor size >3.5cm negatively impacted PFS (HR 1.52, 95% CI 1.08-2.14, p=0.02) and OS (HR 1.93, 95% CI 1.17-3.15, p=0.01). Child-Pugh class B/C was associated with poorer PFS (HR 2.04, 95% CI 1.32-3.15, p<0.01) and OS (HR 3.42, 95% CI 1.99-5.88, p<0.01). Recurrent status before treatment negatively influenced OS (HR 1.76, 95% CI 1.08-2.87, p=0.02).
Conclusions: Elevated AFP levels, larger tumor size, poorer liver function, and recurrent status were identified as significant prognostic factors for HCC patients treated with CIRT. These findings can guide patient selection and inform potential strategies for improving outcomes, such as considering adjuvant therapy for high-risk patients.

O-6
10163

Contour Prognostic Model: Effect of Diameter and Number of Hepatocellular Carcinomas on Survival after Resection, Trans-Arterial Chemoembolization, and Ablation (The Liver Cancer Study Group of Japan)

Yoshikuni Kawaguchi[1,2], Kiyoshi Hasegawa[1,2], Yasuhiro Hagiwara[2], Mario De Bellis[2], Simone Famularo[2], Elena Panittieri[2], Yutaka Matsuyama[2], Ryosuke Tateishi[2], Tomoaki Ichikawa[2], Takashi Kokudo[2], Namiki Izumi[2], Shoji Kubo[2], Michiie Sakamoto[2], Shuichiro Shiina[2], Tadatoshi Takayama[2], Osamu Nakashima[2], Takamichi Murakami[2], Jean-Nicolas Vauthey[2], Masatoshi Kudo[2], Norihiro Kokudo[2]
[1]Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, The University of Tokyo, [2]The Liver Cancer Study Group of Japan and International Multi-institutions, Japan

Background: Survival after resection, trans-arterial chemoembolization (TACE), and ablation is assessed using diameter and number of hepatocellular carcinoma (HCC) as dichotomous variables, resulting in an underestimation of risk variation. The aim of our report is to develop and validate a new prognostic model for the patient groups using largest diameter and number of HCCs as continuous variables.
Methods: The prognostic model was developed based on diameter and number of HCCs as continuous variables using data from patients undergoing resection, TACE, and ablation in 645 Japanese institutions. The models were shown after balanced with the inverse probability of treatment weighted (IPTW) analysis and were externally validated in an international multi-institution cohort.
Results: Of 77,268 patients, 43,904 patients including 15,313 (34.9%) undergoing liver resection, 13,375 (30.5%) undergoing TACE, and 15,216 (34.7%) undergoing ablation met the inclusion criteria. Our model showed that the 5-year overall survival (OS) in HCC patients undergoing these interventions decreased with progressive incremental increases in diameter and number of HCCs (Figure 1). The IPTW-adjusted 5-year OS in patients undergoing surgery was 10-20% higher compared to patients undergoing TACE for one to six HCC lesions < 10 cm and were also 10-20% higher compared to patients undergoing ablation for HCC diameter, 2-3 cm. For patients undergoing resection and TACE, the model performed well in the external cohort.
Conclusion: Our novel prognostic model performed well in predicting OS after resection and TACE for HCC and supports the treatment selection of HCC in clinical practice.

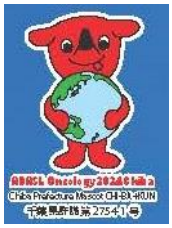
APASL Oncology 2024 Chiba

"Genomics Meets Immunology:

Interdisciplinary Approach for Liver Cancer"

Abstracts

Poster Sessions



Poster Session

P-01
10019

An Effective Prognostic Risk Model Related to Fatty Acid Metabolism in Hepatocellular Carcinoma

Xiaobin Li[1], Shiping Hu[2]
[1]Beijing University of Chinese Medicine, China, beijing, [2]Shenzhen Hospital, Beijing University of Chinese Medicine, China

Background: Evidence increasingly suggests that hepatocellular carcinoma (HCC) is characterized by alterations in fatty acid metabolism. It remains unclear whether fatty acid metabolism-related genes (FAMRGs) exert an influence on HCC. This study aimed to elucidate the relationship between FAMRGs and HCC, and developing a robust prognostic model based on the expression profiles of FAMRGs.
Methods: Based on the differences in the expression of FAMRGs, patients with HCC were divided into different clusters by consensus clustering. A prognostic risk model was created based on differentially expressed genes (DEGs) identified within FAMRG-clusters. We investigated the variations in overall survival rates, the immune infiltration, the tumor microenvironment score, gene mutation characteristics and drug sensitivity between high- and low-risk groups in HCC patients. Lastly, immunohistochemistry staining was employed to validate the expression of prognostic risk genes in HCC.
Results: HCC patients were classified into three FAMRG-clusters. Following this, we identified four prognostic risk DEGs among three FAMRG-clusters and constructed a prognostic risk model. Next, patients were stratified into high- and low-risk groups. The high-risk group exhibited poorer overall survival rates, an immunosuppressive tumor microenvironment, and reduced sensitivity to anti-cancer therapies. Additionally, immunohistochemical staining revealed significant differences in the expression of prognostic risk genes between HCC tissues and normal tissues.
Conclusion: This study constructed a prognostic risk model based on the expression patterns of FAMRGs and elucidated the relationship between fatty acid metabolism and the prognosis of HCC. The four-gene risk model may be a critical tool for the prognostic assessment of HCC.

P-02
10042

Potential Correlation between Changes in Serum FGF21 Levels and Lenvatinib-Induced Appetite Loss in Patients with Unresectable Hepatocellular Carcinoma

Risako Kohya, Goki Suda, Masatsugu Ohara, Takashi Sasaki, Takashi Kitagataya, Masato Nakai, Takuya Sho, Koji Ogawa, Naoya Sakamoto
Department of Gastroenterology and Hepatology, Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Background: Lenvatinib, used for unresectable hepatocellular carcinoma (HCC), causes appetite loss, but the underling mechanisms and impact are unclear. FGF21, linked to cachexia, modulates appetite. We analyzed the effect of appetite loss during Lenvatinib on prognosis and its association with changes in FGF21 levels.
Methods: This retrospective study included unresectable HCC patients who initiated Lenvatinib between 2018 and 2021. FGF21 levels were analyzed at baseline and 1, 2, and 4 weeks after Lenvatinib initiation, and prior to appetite loss onset. We assessed the prevalence of appetite loss, its effect on PFS, OS, liver function, and serum albumin levels. The association between FGF21 level changes and appetite loss was also examined.
Results: A total of 63 patients were included. Appetite loss occurred in a median of 21.5 days after treatment initiation. Grade ≥2 appetite loss was observed in 22 % of patients. This led to deteriorated liver function and shorter OS (median OS, 8.5 vs. 15.0 months; HR: 2.763, $p = 0.007$). Baseline characteristics and serum FGF21 levels were similar between patients with and without appetite loss. However, the rate of change in serum FGF21 significantly increased at 4 weeks after initiation in patients with grade ≥2 appetite loss ($p = 0.0094$) and prior to its onset ($p = 0.0384$).
Conclusions: The rate of change in serum FGF21 significantly increases prior to the onset of grade ≥2 appetite loss. These findings suggest that changes in serum FGF21 could serve as a predictive factor for severe appetite loss during Lenvatinib treatment.

P-03
10065

The Importance of Assessing Energy Malnutrition in Atezolizumab/Bevacizumab Therapy

Maho Egusa[1], Issei Saeki[1], Tsuyoshi Fujioka[1], Norikazu Tanabe[1], Takahiro Yamasaki[2], Taro Takami[1]
[1]Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine,
[2]Department of Oncology and Laboratory Medicine, Yamaguchi University Graduate School of Medicine

Background: Patient's general condition is an important factor independent of tumor progression or hepatic reserve function in HCC. We focused on energy malnutrition as nutritional assessment.
Methods: We included 58 patients received atezolizumab/bevacizumab therapy who were measured non-protein respiratory quotient (npRQ) using an indirect calorimeter.
Results: The median age was 76 years and 45 were men. Regarding liver function and BCLC stage, Child-Pugh class A/B/C were 50/8/0, and BCLC stage A/B/C were 1/33/24. 45 patients treated with 1st-line. The median npRQ was 0.82, and was used as cutoffs. The ORR and DCR was 31.0% and 81.0%, respectively, Median OS and median PFS were 23.5 and 9.6 months, respectively. There was no significant difference in patient background between high and low npRQ. PFS was similar between high and low npRQ, but high npRQ tended to have better OS (24.5 vs. 22.4 months, p=0.067) and survival after treatment failure (SATF) (22.1 vs. 11.6 months, p=0.034). We performed subanalysis according to BCLC stages-AB and C. In the BCLC-C group, PFS, OS, and SATF were comparable for high and low npRQ. In contrast, in the BCLC-AB group, high npRQ showed better OS (24.5 vs. 22.8 months, p=0.018), PFS (13.8 vs. 7.7 months, p=0.342), and SATF (22.1 vs. 16.8 months, p=0.063) all in patients with high npRQ. On multivariate analysis, npRQ was an independent prognostic factor in the BCLC-AB group (HR 3.52, p=0.019).
Conclusions: Low npRQ was a poor prognostic factor in Atezo/Bev for HCC patients with BCLC-AB.

P-04
10114

Understanding the Disease Stage of Intermediate Stage Hepatocellular Carcinoma (HCC) - Analysis of Initial Treatment and Tumor Conditions

Teppei Akatsuka, Sadahisa Ogasawara, Makoto Fujiya, Takahiro Tsuchiya, Midori Sawada, Ryo Izai, Chihiro Miwa, Takuya Yonemoto, Tadayoshi Kogure, Sae Yumita, Hiroaki Kanzaki, Keisuke Koroki, Masanori Inoue, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Shingo Nakamoto, Naoya Kato
Department Gastroenterology, Graduate School of Medicine, Chiba University, Japan

Objective: Transarterial chemoembolization (TACE) is the standard treatment for intermediate-stage hepatocellular carcinoma (HCC). However, some patients can achieve cancer-free status with surgical resection, ablation, or drug therapy. This study analyzed cancer-free rates based on initial treatment methods, tumor conditions, tumor distribution, and gross classification using our hospital's database.
Methods: We reviewed outcomes for intermediate-stage HCC cases diagnosed at our hospital from 2004 to 2022. Cancer-free status was defined as being recurrence-free for at least 6 months after radical therapy or showing complete response (CR) by TACE or drug therapy according to modified RECIST.
Results: Out of 913 patients, 149 (16.3%) achieved cancer-free status. Of these, 28/149 (18.8%) achieved this after surgical resection, 7/149 (4.7%) after drug therapy, and 75/149 (50.3%) after TACE. Tumor conditions included greater than or equal to 8 tumors in 18/149 (12.1%), central distribution in 43/149 (28.9%), and invasive type in 43/149 (28.9%). makes it much harder.
Conclusions: Resection and ablation were associated with higher cancer-free rates. For patients with greater than or equal to 8 tumors, achieving cancer-free status is more difficult, so treatment strategies should account for this.

P-05
10117

Analysis of Immune-mediated Adverse Event Colitis Induced by Combination Therapy with Durvalumab and Tremelimumab for Advanced Hepatocellular Carcinoma

Makoto Fujiya, Sadahisa Ogasawara, Midori Sawada, Takahiro Tsuchiya, Teppei Akatsuka, Ryo Izai, Chihiro Miwa, Takuya Yonemoto, Sae Yumita, Ryuta Kojima, Hiroaki Kanzaki, Keisuke Koroki, Masanori Inoue, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Shingo Nakamoto, Naoya Kato
Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

Background: Durvalumab-tremelimumab combination therapy (STRIDE regimen) is used for advanced hepatocellular carcinoma (HCC), but often causes immune-mediated adverse events (imAEs). Regimens including anti-CTLA-4 antibodies are associated with a high incidence of diarrhea. This study aimed to investigate the clinical characteristics of imAE colitis induced by STRIDE therapy in our hospital.
Methods: We retrospectively analyzed 68 patients who received STRIDE therapy for advanced HCC at our hospital from April 2023 to March 2024. Patient demographics, incidence and severity of diarrhea, treatment interventions, and outcomes were evaluated.
Results: The median age was 74 years (range: 35-85), with 58 males (85%). Diarrhea occurred in 21 patients (31%), with a median onset of 16 days (range: 2-69) after treatment initiation. CTCAE grades were: Grade 1 in 8 (12%), Grade 2 in 5 (7%), Grade 3 in 6 (9%), and Grade 4 in 2 (3%) patients. While 10 cases resolved with symptomatic treatment, 11 required systemic steroids, including 3 needing infliximab. All cases of Grade 3 and 4 underwent lower gastrointestinal endoscopy. The median time from onset to steroid initiation was 8 days (range: 0-11).
Conclusions: The incidence of imAE colitis in our study was comparable to previous reports. Early intervention with steroids and consideration of infliximab for steroid-resistant cases is crucial for managing this significant complication in HCC immunotherapy.

P-06
10126

Pathophysiology of Immune Related Liver Injury from a Clinicopathological Perspective

Ryo Izai[1], Sadahisa Ogasawara[1], Makoto Fujiya[1], Teppei Akatsuka[1], Midori Sawada[1], Takahiro Tsuchiya[1], Chihiro Miwa[1], Takuya Yone[1], Sae Yumita[1], Keisuke Koroki[1], Masanori Inoue[1], Naoya Kanogawa[1], Masato Nakamura[1], Takayuki Kondo[1], Shingo Nakamoto[2], Mina Komuta[2], Naoya Kato[1]
[1]Department of Gastroenterology, Graduate School of Medicine, Chiba University, [2]Department of Daiagnostic Pathology, International University of Health and Welfare Narita Hospital, Japan

Background: As immune checkpoint inhibitors (ICIs) are used in various cancer types, the frequency of immune-related liver injury (irLI) is increasing. However, few reports adequately examine the clinical course and pathological findings of liver biopsy specimens taken at the time of irLI. Therefore, we investigated the clinical course and pathological findings of liver biopsy specimens obtained at our institution during irLI.
Methods: We investigated the clinicopathological characteristics of patients who received ICIs at our institution and underwent liver biopsy for suspected irLI.
Results: Twenty-one cases were included in the analysis. The carcinomas included hepatocellular carcinoma (HCC) in 11 cases, kidney cancer in 4 cases, lung cancer in 2 cases, and skin cancer, sinus cancer, esophageal cancer, and breast cancer in 1 case each. Fifteen cases had Grade 3 or higher AST/ALT elevation, and 13 were treated with steroids. Pathological findings showed hepatitis type in 18 cases (85.7%), bile duct type in 2 cases, and mixed type in 1 case. Of the 11 patients with chronic liver disease (CLN), 9 had Grade 3 or higher AST/ALT elevation. In 6 of the HCC cases, we accurately assessed the degree of inflammation by comparing the pathological findings with those of the background liver before the start of ICI.
Conclusion: IrLI was predominantly of the hepatitis type. In particular, 80% of patients with CLN had Grade 3 or higher AST/ALT elevation. In HCC patients with chronic liver disease, comparing liver biopsies before and during irLI may be useful for accurate diagnosis.

P-07
10150

Sorafenib Induced Stevens-Johnson Syndrome after Immune Checkpoint Inhibitor Treatment in a Patient of Hepatocellular Carcinoma

Kosuke Kojima[1], Tomoaki Yoshida[1], Toru Kawai[2], Naruhiro Kimura[1], Takeshi Yokoo[1], Riichiro Abe[2], Shuji Terai[1]
[1]Department of Gastroenterology, University of Niigata, Niigata, Japan, [2]Dermatological Department, University of Niigata, Niigata, Japan

Background: Sorafenib induced stevens-johnson syndrome (SJS) is rare. Here, we present a case of hepatocellular carcinoma (HCC) with sorafenib-induced SJS after immune checkpoint inhibitor treatment which is a relatively new therapeutic option for HCC and can induce immune cell-mediated adverse events.
Case: 73-year-old man suffered from recurrent multiple HCC after extended posterior segmentectomy. One month of lenvatinib treatment as first-line and three times treatment of durvalumab/tremelimumab as second-line resulted in liver tumor progression and lung metastasis, therefore sorafenib was initiated as third-line treatment. On day 14 of sorafenib administration, he developed eye bloodshot, systemic-, infiltrative-erythema with blisters, and was diagnosed with SJS pathologically. Therefore, he received sorafenib discontinuation and 1mg/kg dose of methylprednisolone, resulting in successful recovery from SJS. Because sorafenib was identified as the cause of SJS with a high stimulation index of drug-induced lymphocyte stimulation test (DLST) to sorafenib, he received another ICI treatment of atezolizumab/bevacizumab as a fourth-line treatment without SJS recurrence.
Conclusion: Previous reports suggested ICI can induce severe skin manifestation like SJS during or after treatment. Supportingly, only one case of sorafenib-induced SJS was reported until the approval of ICI as an anti-cancer treatment though, three cases including this case with SJS induced by sorafenib after ICI has already been reported, indicating ICI might enhance the immunological response to sorafenib which is originally inducible of skin-related adverse events. Giving that, we should pay more attention to severe skin manifestations of sorafenib after ICI treatment.

P-08
10012

Solanum Torvum Induces Ferroptosis to Suppress Hepatocellular Carcinoma through Suppression of GPX4 and Activation of HO-1

Hsiang-Chun Lai[1], Ju-Chien Cheng[2], Sheng-Teng Huang[3,4,5]
[1]Graduate Institute of Chinese Medicine, School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan, [2]Department of Medical Laboratory Science and Biotechnology, China Medical University, Taichung, Taiwan, [3]Department of Chinese Medicine, China Medical University Hospital, Taichung, Taiwan, [4]School of Chinese Medicine, China Medical University, Taichung, Taiwan, [5]Cancer Research Center for Traditional Chinese Medicine, Department of Medical Research, China Medical University Hospital, Taichung, Taiwan

Background: *Solanum torvum* Sw. (ST; folk name: wan-tao-hua) has traditionally been used for common cold, chronic gastritis, and tumors in folk medicine. This study aimed to demonstrate that ST induced ferroptosis in hepatocellular carcinoma (HCC), the combination effect with lenvatinib, and the impact on lenvatinib-resistant cells.
Methods: Cell viability assays were determined using different hepatoma cell lines. Lipid peroxidation and iron assays were performed using flow cytometry. Molecules related to the ferroptosis pathway were detected by western blotting. Finally, a lenvatinib-resistant Hep 3B cell line (Hep 3B-LR) was established to evaluate the antiproliferative effects of ST.
Results: ST ethanol extract inhibited cell growth in various hepatoma cell lines. A dose dose-dependent, significant decreased in glutathione peroxidase 4 (GPX4) expression and increased in acyl-CoA synthetase long-chain family member 4 (ACSL4) were observed after ST treatment, which was accompanied by increased lipid peroxidation. Furthermore, ST induced ferrous iron accumulation mainly through heme oxygenase-1 (HO-1) expression, leading to ferroptosis. ST and lenvatinib combination showed an additive effect (combination index: 0.97). In a lenvatinib-resistant cell line, ST retained its potential anti-HCC efficacy compared to parental Hep 3B cells.
Conclusion: This study demonstrated that the ethanol extract of ST inhibits HCC cell growth by inducing multiple ferroptosis-related pathways. ST displayed an additive effect with lenvatinib in Hep 3B cells and showed remarkable anti-HCC activity in Hep 3B-LR. Collectively, the study suggested that ST might have the potential to reduce lenvatinib use in clinical practice and salvage patients with lenvatinib-resistant HCC.

P-09
10018

Chai Qi Yi Gan Granule Restores Gut Microbial Balance and Modulates Lipid Metabolism to Suppress Hepatocellular Carcinoma

Xiaobin Li[1], Shiping Hu[2]
[1]Beijing University of Chinese Medicine, China, Beijing, [2]Shenzhen Hospital, Beijing University of Chinese Medicine, China

Background: Evidence increasingly suggests that harmful gut microbiota and metabolites in hepatocellular carcinoma (HCC) patients may contribute to HCC progression. Chai Qi Yi Gan Granule (CQYG) has been widely utilized in the treatment of patients with HCC. This study aims to reveal the alterations and functions of gut microbiota and its correlation with the fecal metabolome in the process of improving HCC with CQYG.
Methods: The effects of CQYG in H22 tumor-bearing mice were assessed using tumor weight measurements, HE staining, and TUNEL assays. 16S rRNA sequencing and multi-metabolomics were performed to analyze the alterations in the gut microbiota and fecal metabolism. The correlation between differential microbial communities in the gut and differentially fecal metabolites was analyzed using Spearman's correlation analysis.
Results: The pharmacodynamic evaluations demonstrated that CQYG inhibited HCC tumor growth, promoting HCC cellular apoptosis significantly, and effectively mitigating colon tissue injury. Moreover, CQYG reversed HCC-induced gut microbiota dysbiosis by elevating the abundance of Bacteroides and Muribaculaceae, while reducing the abundance of Desulfovibrio and Incertae_Sedis. Furthermore, CQYG also reversed the HCC-induced metabolic disorder by regulating the glycerophospholipid and sphingolipid metabolism, and correlation analysis showed that lipids and lipid-like molecules were closely related to distinct gut microbiota.
Conclusion: Gut microbiota and fecal metabolism might be a target of CQYG in the process of ameliorating HCC. Our findings provide novel insight into the mechanisms underlying the effects of CQYG on HCC and contribute to the development of TCM.

P-10
10066

Integrated Single-Cell and Bulk RNA Sequencing Reveals CCR2-High Neutrophils in Gr1+ Myeloid Lineages of CRLM Mice

Zijun Yan, Xiuping Zhang, Gong Zhang, Yanzhe Liu, Zhaoda Deng, Rong Liu
Faculty of Hepato-Biliary-Pancreatic Surgery, The First Medical Center of Chinese People's Liberation Army (PLA) General Hospital, Beijing, China

Background: Colorectal liver metastases (CRLM) are a major factor contributing to tumor recurrence and mortality. Up to 48.1% of colorectal cancer (CRC) patients develop hepatic metastases within three years. During the progression from micro- to macro-metastasis, myeloid lineages are recruited from the bone marrow into the bloodstream and subsequently colonize pre-metastatic niches in response to chemokine signaling. However, the mechanisms by which myeloid-derived cells create an environment conducive to tumorigenesis, characterized by the suppression of anti-tumor immune activity and the promotion of tumor metastasis, remain unclear. Therefore, investigating the underlying mechanisms of CRLM is crucial.
Methods: Liver metastasis was simulated in C57BL/6 mice via splenic injection of MC38 cells. Combining flow cytometry sorting and single-cell sequencing technology, we delineated the cellular atlas of CD11b+/Gr1+ myeloid lineages from the bone marrow of CRLM mice. Critical pathway alterations were validated through bulk RNA sequencing.
Results: This study identified a CCR2-high neutrophil subpopulation within the Gr1+ myeloid cells of CRLM mice. These CCR2+ neutrophils promote the epithelial-mesenchymal transition (EMT) through FN1-CD44 signaling. Subsequently, CCR2+ neutrophils are released into the peripheral blood, exhibiting high expression of TGF-β1 and IL-1β, and promote CRLM through the JAK-STAT signaling pathway.
Conclusions: We discovered a subpopulation of neutrophils with high CCR2 expression in the bone marrow of CRLM mice. Since neutrophils are most often associated with infection, we included single-cell sequencing data from the bone marrow of sepsis mice and did not find CCR2+ neutrophils. Thus, this new cell population may play a pivotal role in the development of CRLM.

P-11
10133

Early Width of Dispersion of Monocytes Complexity (MO-WX) as a Discriminating Tool of Hepatocellular Carcinoma in Liver Cirrhotic: A Pilot Study of Novel Marker with Leukocytes Cell Population Data

Dwijo A Sindhughosa[1], I Putu Y Prabawa[2], I Dewa A G A Janardhana[2], I K Mariadi[1], Anak A W Lestari[3]
[1]Gastroenterology and Hepatology Division, Department of Internal Medicine, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G. Ngoerah Hospital, Bali, Indonesia, [2]Clinical Pathology Residency Education Program, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G. Ngoerah Hospital, Bali, Indonesia, [3]Department of Clinical Pathology, Faculty of Medicine, Udayana University, Prof. Dr. I.G.N.G. Ngoerah Hospital, Bali, Indonesia

Background: Recent advancements in hematological parameters have introduced leukocytes cell population data (CPD) as a promising tool for cancer detection and prognosis. In particular, the early width of dispersion of monocytes complexity (MO-WX) has emerged as a potential novel marker, reflecting changes in monocyte complexity and heterogeneity in response to tumor presence. This pilot study aimed to investigate the MO-WX in patients with HCC, exploring its diagnostic capabilities potential in HCC.
Methods: A cross-sectional study was conducted among 76 liver cirrhotic patients The MO-WX was collected from Sysmex XN series along with complete blood count evaluation. The diagnosis of HCC was confirmed through National Consensus of HCC. Analysis of difference and receiver operating curve (ROC) was performed to obtained the discriminative value of MO-WX for HCC. We also evaluated the optimal cut-off value to predict HCC using Youden Index (YI).
Results: A higher value of MO-WX was observed between between HCC and non-HCC population [266.5 (241-319) ch vs 252.5 (119.9-355) ch, p = 0.032). The ROC analysis yield the Area Under Curve (AUC) of 0.658 for its ability to predict HCC (p = 0.032). Using the optimal cut-off value of 244 ch (YI: 28.79), we obtained sensitivity 95.5%, specificity 33.3%, positive predictive value (PPV) 36.8%, negative predictive value (NPV) 94.7%, and accuracy 51.3%. Moreover, this cut-off was associated with a 10.5-fold increase in HCC probability (p=0.009).
Conclusion: The MO-WX obtained in patients with liver cirrhosis may have a significant impact to discriminate HCC in specific liver cirrhotic population.

P-12
10153

Biflavonoid Derivatives as Potential CDK1 Inhibitors in Hepatocellular Carcinoma: Investigation via Virtual Screening and Molecular Interaction Analysis

Reny Rosalina[1], Rian Ka Praja[2]
[1]Department of Chemistry, Faculty Mathematics and Natural Science, University of Palangka Raya, [2]Faculty of Medicine, University of Palangka Raya

In Hepatocellular carcinoma (HCC), CDK1 expression was elevated, which is positively linked to the malignancy stages. These genes' expression levels correspond with immune cell infiltration and predict HBV-induced hepatocellular cancer outcome. CDK overproduction can induce cancer growth and render traditional chemotherapy ineffective for solid tumors. Thus, CDK1 inhibitors may treat HCC, with some in clinical trials. We sought a natural CDK1 inhibitor, especially biflavonoids.This work implemented a virtual screening technique to investigate the binding of 25 biflavonoid derivative compounds from the ZINC database to the CDK1 binding site. The Autodock Vina software was utilized, followed by molecular interaction analysis conducted using Biovia Discovery Studio. The pharmacological characteristics were evaluated using SwissADME and pkCSM online servers.Out of the 25 compounds derived from biflavonoids, 16 exhibited a more potent binding affinity, shown by the lowest observed binding energy in ZINC000207027026, compared to reference CDK1 inhibitors. The presence of a connection between the aromatic ring and the hydrogen bond acceptor moiety is crucial for the pharmacophore of the chemical ZINC000207027026. Both the pi bonding of the aromatic ring and hydrogen bonding are significant factors in this interaction (Figure 1). Furthermore, it was shown that incorporating non-aromatic substituents into the central structure reduced binding affinity. The chemical ZINC000207027026 has drug-like characteristics according to the Lipinski criteria and ADMET prediction.In summary, biflavonoid exhibits potential as a suitable candidate for CDK1 inhibitors. This study presents noteworthy discoveries in pharmaceutical research, particularly focusing on novel chemicals that specifically target cell cycles for cancer treatment.

Poster Session

P-13 **Withdrawn**
10125

P-14
10049

Dietary Elaidic Acids Promotes Malignant Behavior of HepG2 Cells via NF-kappaB Signaling Pathway

Xiao Hu[1], Ran Guo[2], Rui Hu[3], Gang Li[4], Naoki Tanaka[5], Peici Yan[1], Xiangnan Wang[1]
[1]Department of Pathophysiology, Hebei Medical University, Shijiazhuang , China, [2]The Third General Surgery Department, The Second Affiliated Hospital of Hebei Medical University, Shijiazhuang, China, [3]General Clinical Laboratory, The Second Affiliated Hospital of Hebei Medical University, Shijiazhuang, China, [4]Cardiology Division in Geriatric Institute, Hebei General Hospital, Shijiazhuang China, [5]Department of Metabolic Regulation, Institute on Aging and Adaptation, Shinshu University Graduate School of Medicine, Matsumoto, Japan

Background: Previous studies suggested that consumption of trans-fatty acids (TFAs) is one of the risk factors for MAFLD, while little attention has been paid to HCC. Elaidic acids (EAs), one of the most common TFAs found in commercial foods, were used to treat HepG2 cells aiming to explore the effect of dietary TFAs on hepatic tumor incidence and the mechanisms.
Methods: HepG2 cells were treated with 100μM or 200μM EAs for 24 hours, HCC-associated cellular and molecular phenotypes were examined. Same concentration of BSA and Oleic acid were used as the control.
Results: After EAs treatment, the cellular pseudopods were recovered and body became round, and the cells cluster resemble island shape, suggesting that HepG2 cells were likely to proliferation. CCK8 results showed that EAs enhanced cell survival compared with oleic acid at the same concentration. Annexin V & Dead Cell staining showed that EAs might have the effect of activating caspase and then promoting early apoptosis. Transwell-assay demonstrated that EAs promoted the cell migration ability. The expression levels related to NF-kappaB pathway and its downstream genes which regulate cell proliferation, were significantly elevated after EAs-treated.
Conclusions: EAs could aggravate malignant behavior of hepatoma cells, presumably due to enhancing NF-kappaB pathway. These results indicate the importance of dietary intervention for HCC Prevention.

P-15
10015

Association between Osteosarcopenia and Prognosis in Liver Cirrhosis Complicated with Portal Hypertension

Arisa Saito[1,2], Takuto Nosaka[1], Yosuke Murata[1], Tomoko Tanaka[1], Yu Akazawa[1], Tatsushi Naito[1], Kazuto Takahashi[1], Masahiro Ohtani[1], Yasunari Nakamoto[1]
[1]Second Department of Internal Medicine, Faculty of Medical Sciences, University of Fukui, Fukui, Japan, [2]Fukui General Hospital, Fukui, Japan

Background: With the aging population of patients with liver cirrhosis, improving quality of life is important. Osteosarcopenia is a new concept combining osteoporosis and sarcopenia, and its relationship to the prognosis of cirrhosis is still unclear. We retrospectively examined the association between osteosarcopenia, nutritional markers, and prognosis in cirrhosis patients.
Methods: The subjects were 97 cirrhotic patients with non-ruptured esophageal and gastric varices who underwent endoscopic treatment or B-RTO from 2006 to 2023. Sarcopenia was defined by Psoas Muscle Index(PMI). Based on previous reports, osteopenia was defined as cases with less than Bone Mineral Density(BMD) calculated by CT mean value of the mid-vertebral core at the bottom of 11th thoracic vertebra. Nutritional markers were examined with NLR, PNI, and CONUT. Prognosis was compared in 4 groups: control (C), sarcopenia (S), osteopenia (O), and osteosarcopenia (O+S).
Results: 12 cases(12.4%) were determined to have osteosarcopenia. There was no significant correlation between BMD and PMI ($r=0.084$, $p=0.412$). Median survival was C: 2496 days, S: 1677 days, O: 1159 days, and O+S: 954 days, the prognosis being most significantly worse in the O+S ($p<0.05$). In multivariate analysis, osteosarcopenia, age≥65, Albumin<3.5 g/dL, Na<140 mmol/L, and hepatocellular carcinoma were independent prognostic factors ($p<0.05$). Comparing the O+S and non-O+S, the O+S group was significantly malnutrition (Albumin 3.2 vs 3.5, PNI 34.7 vs 40.7, NLR 3.7 vs 2.0, CONUT 8 vs 4, all $p<0.05$).
Conclusion: In liver cirrhosis patients with portal hypertension, osteosarcopenia is an independent poor prognostic factor, suggesting the importance of maintaining bone mass as well as muscle mass.

P-16
10017

Reasons for Liver Regeneration Failure, How to Save it?

Bowen Liu[1], Fenping Lu[1], Xiaobin Li[1], Shiping Hu[2]
[1]Beijing University of Traditional Chinese Medicine, [2]Shenzhen Hospital of Beijing University of Traditional Chinese Medicine (Long Gang), China

Liver regeneration has been the focus of recent research. Although the mechanism of liver regeneration is well understood, there is little knowledge about liver regeneration failure and how to prevent it. This review summarizes the effects of various factors, such as surgical treatment, lipid droplet deposition, aging, intestinal flora, platelets, nutrition, hormones, etc., on liver regeneration failure. It also explores potential therapeutic strategies that target liver regeneration at the molecular and cellular levels. Additionally, stem cell research, tissue engineering, gene technology, liver organoids, and natural medicine have great potential for promoting liver regeneration.

P-17
10050

Long-term L-carnitine Supplementation Suppresses Skeletal Muscle Mass Loss by Decreasing the Expression of Interleukin-6 in Patients with Hepatocellular Carcinoma

Yu Takeda[1], Koji Sawada[1], Shin Otake[1], Hidemi Hayashi[1], Yu Ota[1], Takumu Hasebe[1], Shunsuke Nakajima[2], Kazunobu Aso[1], Mikihiro Fujiya[1]
[1]Division of Gastroenterology, Department of Internal Medicine, Asahikawa Medical University, Asahikawa, Japan, [2]Department of Emergency Medicine, Asahikawa Medical University, Asahikawa, Japan

Background: The effect of L-carnitine (LCA) on skeletal muscle mass in patients with hepatocellular carcinoma (HCC) is unknown. We evaluated whether long-term LCA supplementation could suppress the loss of skeletal muscle mass in patients with HCC and investigated its underlying mechanism.
Methods: (1) We analyzed 64 patients with HCC treated with or without LCA for more than 12 months. The skeletal muscle mass index (SMI) was calculated, and correlations between the rate of changes in serum ammonia levels and the SMI were analyzed. (2) To elucidate the effect of LCA on HCC, C2C12 cells were cultured in the supernatant of HCC cells treated with LCA. (3) We also analyzed the correlations between the serum IL-6 level and SMI in 55 patients with HCC.
Results: (1) Loss of SMI was significantly suppressed in the LCA group; however, there was no correlation between the rate of change in serum ammonia levels and the SMI. (2) An in vitro study showed that the myotube diameter was significantly larger with LCA supplementation. LCA supplementation down-regulated the expressions of atrogin-1 and cathepsin-L. The IL-6 level in the supernatant was significantly decreased by LCA supplementation. (3) The serum IL-6 level was significantly higher in patients with low SMI. There was a significant positive correlation between the serum IL-6 level and the diameter of HCC.
Conclusion: This study demonstrated that long-term LCA supplementation decreased the expression of IL-6 in HCC and suppressed the loss of skeletal muscle mass in patients with HCC.

P-18
10052

Effect of MAFLD Criteria on Postoperative Recurrence of NBNC-HCC

Yusuke Johira[1], Takashi Nakahara[2], Kenji Yamaoka[1], Yasutoshi Fujii[1], Shinsuke Uchikawa[1], Hatsue Fujino[1], Atsushi Ono[1], Eisuke Murakami[1], Daiki Miki[1], Tomokazu Kawaoka[1], Masataka Tsuge[1], Shiro Oka[1]
[1]Department of Gastroenterology, Hiroshima University Hospital, Hiroshima, Japan, [2]Hiroshima Prefectural Hospital, Japan

Background: It is not clear in which population the complications of MAFLD criteria especially contribute to recurrence after hepatectomy for NBNC-HCC. In this study, we evaluated the usefulness of MAFLD criteria as predictors of postoperative recurrence.
Methods: Of 141 patients who underwent radical hepatectomy as their initial treatment for NBNC-HCC within the Milan criteria, 94 patients with no evidence of vascular invasion, intrahepatic metastasis, or positive resection margins in pathology specimens were included in this study. We examined the factors contributing to postoperative recurrence in the population with or without advanced liver fibrosis respectively, defined as fibrosis stage 3 or 4 in the Brunt classification.
Results: Independent factors contributing to postoperative recurrence in the overall population were being men ($p=0.015$) and complication of diabetes mellitus ($p=0.014$) and advanced liver fibrosis ($p<0.001$). Those in the cases with advanced liver fibrosis (n=43) were non-overweight ($p=0.02$), complication of diabetes mellitus ($p=0.006$), and preoperative AFP level of 8.2 ng/ml or higher ($p=0.021$). On the other hand, in the cases without advanced liver fibrosis (n=51), only complication of all three MAFLD criteria contributed to postoperative recurrence.
Conclusion: MAFLD criteria as well as advanced liver fibrosis was suggested to have certain usefulness as a predictor of postoperative recurrence of NBNC-HCC. In patients without advanced fibrosis, the overlap of MAFLD criteria contributed to recurrence rather than a specific MAFLD factor alone.

P-19
10092

Effectiveness of Multidisciplinary Inpatient Treatment with Personalized Diet and Exercise Therapy for Steatotic Liver Disease

Eriksson Yasuka, Yusuke Kawamura, Shigeki Yamamoto, Hitomi Sezaki, Tetsuya Hosaka, Satoshi Saitou, Fumitaka Suzuki, Hiromitsu Kumada, Norio Akuta
Department of Hepatology Liver Disease Center, Toranomon Hospital, Japan

Background: Data evaluating the combined effects of diet and exercise on SLD are limited. At Toranomon Hospital, the Hospitalization Program for Improvement Purpose for SLD was initiated in June 2021. The purpose of this study is to evaluate the efficacy of this program on liver function, glycolipid metabolism, body weight, and liver stiffness.
Methods: This study included 302 patients diagnosed with SLD by abdominal ultrasonography and who participated in the hospitalization program for SLD at our hospital. All patients underwent personalized diet and exercise treatment. The diet consisted of 25to30 kcal/kg of ideal body weight per day, and aerobic and resistance exercises (exercise intensity of 4to5 metabolic equivalents, respectively) were performed for six days. Treatment efficacy was evaluated by comparing liver function tests, glycolipid metabolism markers, physical findings, and imaging findings at six months with baseline values.
Results: Among the participants, 238 had MASLD,64 had ALD + MetALD, 60 had HBV, 55 had HCV, 5 had AIH, and 8 had PBC. Six months after hospitalization for SLD improvement, the improvement rates were as follows: AST 56.9%, ALT 64.9%, γGTP 70.5%, HbA1c 66.4%, Total Cholesterol 52.2%, Triglycerides 66.7%. body weight 67.7%, Liver Stiffness measurement by FibroScan 62.9%, and CAP 57.5%.
Conclusion: The personalized diet and exercise program for SLD improved liver function, glycolipid metabolism, body weight, and liver stiffness. Continued evaluation is necessary to understand the long-term impact on liver-related events and cardiovascular events.

P-20
10156

Virtual Screening of Resveratrol-derived Compounds for Targeting the TGF-β1 Receptor in Liver Fibrosis

Rian Ka Praja[1], Reny Rosalina[2]
[1]Faculty of Medicine, Universitas Palangka Raya, Palangka Raya, Indonesia, [2]Faculty of Mathematics and Natural Sciences, Universitas Palangka Raya

Liver fibrosis is a progressive condition characterized by the abnormal accumulation of extracellular matrix (ECM), which can ultimately result in liver damage and cirrhosis. The TGF-β1 signaling pathway is crucial in initiating and advancing this fibrosis by activating hepatic stellate cells (HSCs) and increasing ECM production. With the current therapeutic options being insufficient, there is a strong need for new and effective treatments. This study aimed to evaluate natural bioactive compounds targeting the TGF-β1 receptor as potential treatments for liver fibrosis. We utilized virtual screening methods to find potential TGF-β1 receptor inhibitors from bioactive compounds derived from resveratrol and to analyze their mechanisms of action. Nine natural compounds, known for their antioxidant, anti-inflammatory, and antifibrotic effects, were screened and docked using AutoDockTools. We also assessed their absorption, distribution, metabolism, excretion, and toxicity (ADMET) through the online pkCSM tool to evaluate their drug-like characteristics. All resveratrol derivatives showed binding energies ranging from -8.7 to -11.3 kcal/mol, which were lower than the -7.5 kcal/mol observed for galunisertib, a known TGF-β1 receptor inhibitor. These compounds interacted with the TGF-β1 receptor primarily through hydrophobic interactions with the aromatic ring and hydrogen bonding with oxygen groups. Furthermore, the resveratrol derivatives displayed favorable drug-like properties according to ADMET predictions. In conclusion, the resveratrol derivatives appear to be promising candidates for inhibiting the TGF-β1 receptor. These findings suggest that resveratrol derivatives could be valuable in TGF-β1 inhibition and highlight the potential of using naturally occurring compounds from common foods as treatments for fibrosis.

P-21
10144

Mathematical Modelling for Investigating the Inconsistencies between Transient Elastography and Liver Biopsy Results in Assessing Liver Fibrosis in Patients with Chronic Viral Hepatitis

Prihantini Prihantini[1], Andi Nursanti Andi Ureng[2], Rifaldy Fajar[3]
[1]Machine Learning for medicine Laboratory, Bandung Institute of Technology, Indonesia, [2]Department of Pharmacy, Andini Persada College of Health Sciences, Indonesia, [3]Computational Biology and Medicine Laboratory, Yogyakarta State University, Indonesia

Assessing liver fibrosis in chronic viral hepatitis patients is critical for monitoring disease progression and guiding treatment. Transient elastography (TE) and liver biopsy (LB) are commonly used methods. However, inconsistencies between them results pose challenges in clinical decision-making, patient heterogeneity, and technical limitations. This model offers a way to quantify these discrepancies by integrating data from both methods, simulating various scenarios, and identifying key variables influencing assessments. This approach aims to reconcile differences, improving the accuracy and reliability of fibrosis evaluation and enhancing patient outcomes.A comprehensive dataset of liver stiffness measurements and biopsy scores from chronic viral hepatitis patients are processed. By handling the missing values, normalising measurements, and categorising fibrosis stages can simulate fibrosis progression and assess the impact of clinical and demographic factors on test outcomes. Cross-validation ensured robustness and accuracy in identifying contributors to inconsistencies.TE often overestimates fibrosis in early stages and underestimates it in advanced stages compared to LB. Significant factors affecting these discrepancies included patient age, body mass index (BMI), and liver inflammation. TE measurements were particularly sensitive to BMI, leading to variances in fibrosis assessment. The correlation between TE and LB varied across patient subgroups, with lower sensitivity but higher specificity in obese patients. Cross-validation confirmed model robustness, with low average prediction errors. These results emphasise the need for personalised interpretation of TE results, considering patient-specific factors like BMI and liver inflammation to enhance liver fibrosis evaluation accuracy in clinical practice.

P-22
10051

A Resected Case of Hepatocellular Carcinoma with Paraneoplastic Syndrome

Mai Totsuka[1], Ryota Masuzaki[1], Masayuki Honda[1], Tomohiro Kaneko[1], Shuhei Arima[1], Naoki Matsumoto[1], Hiroaki Yamagami[1], Shunichi Matsuoka[1], Osamu Aramaki[2], Ryusuke Tsujimura[4], Sumie Ohni[3], Shinobu Masuda[3], Yukiyasu Okamura[2], Hirofumi Kogure[1]
[1]Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan, [2]Division of Digestive Surgery, Department of Surgery, Nihon University School of Medicine, Tokyo, Japan, [3]Division of Oncologic Pathology, Department of Pathology and Microbiology, Nihon University School of Medicine, Tokyo, Japan, [4]Division of Human Pathology, Department of Pathology and Microbiology, Nihon University School of Medicine, Tokyo, Japan

Hepatocellular carcinoma (HCC) is often accompanied by paraneoplastic syndrome. A 70-year-old male was referred to our hospital for the evaluation of liver mass. The patient had been experiencing a high fever and appetite loss for more than three months and also had diabetes mellitus. Initially, he was suspected of having a liver abscess and was treated with antibiotics, but there was no improvement in his condition. Laboratory tests showed abnormal results, including WBC of 22400/μL (BAND 1%, SEG 91%), total bilirubin of 0.50 mg/dL, albumin of 1.8 g/dL, CRP of 19.4 mg/dL, AFP of 517 ng/mL, and PIVKA-II of 66 mAU/mL. A CT scan revealed a 10cm diameter tumor in the right posterior segment with early enhancement and late washout. Although HCC with abscess was initially suspected, antibiotics had no effect. Repeating blood cultures were negative. The patient underwent a hepatectomy, and fever and inflammation were resolved after the surgery (WBC and CRP were 7000/μL and 0.879 mg/dL, respectively). The surgical pathology showed moderately to poorly differentiated HCC in a non-cirrhotic liver. The patient was able to be discharged. Paraneoplastic syndrome of HCC was known to have hyper potassium, hypoglycemia, hypercholesteremia, and polycythemia. Tumor fever is rare and occurs with poorly differentiated HCC or tumor necrosis. Chemical mediators are reported to play a vital role in high fever. The serum level of G-CSF was 87.0 pg/mL and was stained negative by immunohistochemistry. High fever and systemic inflammation can be found in HCC and should be considered in the differential diagnosis.

P-23
10056

A Case of Hepatic Leiomyosarcoma Diagnosed through Autopsy

Kensho Kubo[1], Atsushi Yoshimoto[1], Sera Sawaguchi[1], Yuko Sugawara[1], Ayaka Satou[2], Sadahide Ono[3], Ken Yoshida[1]
[1]Iwate Prefectural Miyako Hospital, Iwate, Japan, [2]Department of Molecular Diagnostic Pathology, Iwate Medical University School of Medicine, Iwate, Japan, [3]Iwate Prefectural Central Hospital, Iwate, Japan

Background: Primary hepatic leiomyosarcoma is a rare disease, accounting for only 0.004% of primary liver cancers. It often presents with limited clinical findings and lacks specific tumor markers, making diagnosis challenging. Here, we report a case of primary hepatic leiomyosarcoma that was diagnosed through autopsy after not being definitively diagnosed during the patient's lifetime.
Methods: The patient was an 83-year-old male who presented with abdominal pain. Contrast-enhanced CT and contrast-enhanced MRI both revealed a large hepatic tumor, but tumor markers such as CEA, CA19-9 and AFP were negative. Endoscopy showed no evidence of gastrointestinal tumors. A liver biopsy was performed to investigate the primary site of the unknown cancer. The biopsy revealed atypical cells with irregularly shaped nuclei and pale cytoplasm diffusely infiltrating the liver, suggesting malignancy, but it was not clear whether it was an epithelial or mesenchymal tumor. The patient died eight months after the initial visit, and an autopsy was conducted.
Results: The autopsy revealed a large, solid tumor occupying the entire right lobe of the liver, with areas of necrosis. Histologically, spindle-shaped to irregularly shaped atypical cells and large bizarre nuclei were observed. Immunohistochemical staining showed cytokeratin (-), α-SMA (+), and caldesmon (+). The tumor was negative for epithelial markers and KIT, but positive for α-SMA, leading to a diagnosis of leiomyosarcoma according to the WHO Classification of Tumors of the Digestive System.
Conclusion: Although primary hepatic leiomyosarcoma is a rare disease, further accumulation of case reports is necessary to establish diagnostic and therapeutic strategies.

P-24
10079

A Case of Hilar Bile Duct Carcinoma with Severe Eosinophilia

Terunao Iwanaga[1], Hidehiro Kamezaki[1], Wei Yang[1], Daiki Tada[1], Kenta Tada[1], Takahiro Maeda[1], Junichi Senoo[1], Kensuke Sugiura[2], Yutaka Sato[2], Atsuhiko Ueda[2], Daiki Okamura[2], Satoshi Kuboki[2]
[1]Department of Gastroenterology, Eastern Chiba Medical Center, Chiba, Japan, [2]Department of General Surgery, Eastern Chiba Medical Center, Chiba, Japan

Introduction: Tumor-associated blood eosinophilia (TABE) rarely occurs in solid cancers. Although it has been reported that TABE is related to tumor progression and prognosis, the detailed mechanism remains unknown. In this study, we report our experience with a rare case of hilar bile duct carcinoma with TABE that required differentiation from eosinophilic cholangitis.
Case Summary: A 72-year-old male was referred to our hospital for further examination and treatment of elevated liver enzymes. Blood tests revealed leukocytosis (WBC 13,490 /mm^3) with marked eosinophilia (eosinophils 9,457 /mm^3). Enhanced CT showed wall thickening of the hilar bile duct and intrahepatic bile duct dilatation. Endoscopic trans-papillary biliary biopsy and stenting were performed. Corticosteroids were started with a clinical diagnosis of eosinophilic cholangitis. Adenocarcinoma was detected in biopsy specimens taken from the bile duct stricture, leading to a diagnosis of hilar bile duct carcinoma. There was no evidence of eosinophilic infiltration in the biopsy specimens. Eosinophilia was thought to be TABE. Left liver lobe and caudate lobe resection, extrahepatic bile duct resection, and choledocho-jejunostomy were performed. Pathological examination showed moderately differentiated adenocarcinoma (T2aN0M0 Stage II).
Conclusion: Bile duct stricture with eosinophilia can be differentiated from cholangiocarcinoma, eosinophilic cholangitis, and other conditions. It is difficult to distinguish them by blood tests or imaging studies alone, and biopsy is necessary for a definitive diagnosis.

P-25
10109

A Case of Hepatic Reactive Lymphoid Hyperplasia Diagnosed by Post-RFA Biopsy Specimen

Masaki Kawabata, Tasuku Nakabori, Kaori Mukai, Kazuyoshi Ohkawa
Osaka International Cancer Institute, Osaka, Japan

Hepatic reactive lymphoid hyperplasia (RLH), also called hepatic pseudolymphoma, is a rare condition. Hepatic RLH is often diagnosed as a suspected hepatocellular carcinoma (HCC) or cholangiocellular carcinoma (CCC) that has been resected, because the contrast effect patterns resemble those of HCC or CCC. Thus, diagnostic method for hepatic RLH is still controversial. Herein, we reported a case of hepatic RLH diagnosed by post-RFA biopsy specimen. A female patient in her 70s came to our hospital for a detailed examination of a 10-mm hepatic nodule. She had ulcerative colitis (UC). Both hepatitis B and C virus-related markers were negative. Tumor markers including alpha-fetoprotein and des-γ-carboxyprothrombin were not elevated. Contrast-enhanced CT and EOB-MRI revealed the nodule enhanced poorly in the arterial phase and delayed phase. Contrast-enhanced US (CEUS) showed the tumor exhibited hyperenhancement in the arterial phase, washout in the portal phase, and defect in the Kupffer phase. Although these findings suggested the nodule was suspected to be HCC, CCC could not be completely denied due to her comorbidity of UC. Thus, we performed RFA for the nodule, followed by biopsy. Histological findings showed clusters of hematoxylinophilic round cells. Immunohistochemical analysis revealed distribution of CD3-positive T cells, CD20-positive B cells, and CD21-positive follicular dendritic cells are in accordance with their physiological condition, and Ki-67-positive cells were localized in the germinal center. Collectively, the nodule was diagnosed as hepatic RLH. Because the clinical significance of post-ablation biopsy is still unclear, we report this case along with a brief literature review.

P-26
10111

Cytokine Release Syndrome Caused by the Combination Immunotherapy for Advanced Hepatocellular Carcinoma

Sae Yumita, Sadahisa Ogasawara, Makoto Fujiya, Teppei Akatsuka, Ryo Izai, Midori Sawada, Takahiro Tsuchiya, Chihiro Miwa, Takuya Yonemoto, Keisuke Koroki, Masanori Inoue, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Shingo Nakamoto, Naoya Kato
Department of Gastroenterology, Graduate School of Medicine, Chiba University, Japan

Background: Cytokine release syndrome (CRS) is a systemic inflammatory disease characterized by a massive release of cytokines. CRS has been reported as an immune-related adverse event associated with immune checkpoint inhibitors. We report three cases of CRS that developed the initiation of combination immunotherapy for advanced HCC.
Case Report: Case1 is a 35-year-old woman who started treatment with the combination therapy of durvalumab plus tremelimumab (STRIDE regimen). She developed grade4 CRS 29 days after the initial dose. We initially suspected sepsis and administered antibiotics, but due to poor treatment response, we suspected CRS and started steroid pulse therapy. Although her condition temporarily improved, CRS recurred when the steroids were tapered. We administered tocilizumab and she made a complete recovery. Case 2 is a 81-year-old man who received the STRIDE regimen. He presented to the outpatient clinic with fever and did not respond to the initial antibiotic treatment. We diagnosed Grade 2 CRS and administered tocilizumab. The fever has since disappeared. He is currently resuming the STRIDE regimen, but CRS has not recurred. Case 3 is a 63-year-old man who was administered the combination therapy of atezolizumab plus bevacizumab. He came to the hospital with a fever of 39 degrees celsius and respiratory distress, with a diagnosis of grade 4 CRS and acute respiratory distress syndrome. We started steroid therapy (1mg/kg/day), which led to an improvement in his condition. Antibiotics were co-administered until sepsis was ruled out.
Conclusion: CRS is a potentially fatal yet treatable condition with appropriate therapeutic interventions.

P-27
10006

A Case of Hepatocellular Carcinoma that could be Radically Resected after Combined Therapy with Lenvatinib and TACE

Ryo Yano, Masashi Hirooka, Yoshiko Nakamura, Toyoki Shimamoto, Makoto Morita, Yuki Okazaki, Yusuke Imai, Takao Watanabe, Osamu Yoshida, Yoshio Tokumoto, Masanori Abe, Yoichi Hiasa
Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Touon, Japan

Background: The definitive treatment for massive hepatocellular carcinoma (HCC) is resection. However, the larger the tumor, the smaller the remaining liver, which makes surgery difficult. Therefore, drug therapy is often first performed. Among them, there are only a few cases that can be transferred to conversion surgery.
Methods: We report a case of massive HCC that was treated with Lenvatinib (LEN) and TACE combination therapy and successfully underwent conversion surgery.
Results: The case was a 76 years-old-man. During follow-up for alcoholic liver disorder, an increase in γ-GT was noted. Computed tomography revealed a 13cm HCC in the right lobe, which presented simple nodular morphology. No distant metastasis was observed. The tumor was severely compressing the right portal vein. Alpha-fetoprotein (AFP) was 27.6 ng/mL and protein induced by vitamin K absence II (PIVKA-II) was 212541 mAU/mL. His liver reserve was good, although resection was deemed inappropriate because the residual liver volume was insufficient after resection. He received combination therapy with LEN and TACE because local control with TACE was assumed to be effective for the nodule morphology. Six months after treatment, AFP decreased to 2.3 ng/mL and PIVKA-II decreased to 369 mAU/mL. CT showed tumor shrinkage to 11 cm with extensive necrosis. There was also mild compensatory swelling in the left lobe, thus right lobectomy was performed. The tumor could be removed all at once, and there were no major complications.
Conclusions: Combination therapy with LEN and TACE was an effective strategy for conversion surgery.

P-28
10035

A Case of Consciously Selected LEN-TACE for Unresectable HCC Combined with Acquired Thrombotic Thrombocytopenic Purpura

Tsuyoshi Fujioka[1], Issei Saeki[1], Maho Egusa[1], Natsuko Nishiyama[1], Daiki Kawamoto[1], Ryo Sasaki[1], Tatsuro Nishimura[1], Norikazu Tanabe[1], Toshihiko Matsumoto[1], Tsuyoshi Ishikawa[1], Kaoru Yamamoto[2], Syota Nono[2], Yasuharu Ota[2], Takahiro Yamasaki[3], Taro Takami[1]
[1]Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan, [2]Division of Endocrinology, Metabolism, Hematological Sciences and Therapeutics, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan, [3]Department of Oncology and Laboratory Medicine, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan

Case: A 60s-year-old woman came to clinic with a complaint of fatigue, and she was referred to our hospital because of a liver tumor seen on abdominal ultrasound. She was diagnosed with hepatocellular carcinoma (HCC) with elevated AFP and DCP. Blood tests revealed renal dysfunction, markedly decreased platelet count, and hemolytic anemia with schistocytes. The diagnosis of acquired thrombotic thrombocytopenic purpura (TTP) was made the basis of low ADAMTS13 activity accompanied by positive anti-ADAMTS13 antibodies. Initially, we prioritized the treatment of TTP as a matter of urgency, and plasma exchange, steroid pulse therapy, and caplacizumab injection were administered. In addition, rituximab was added during the course of the treatment, and TTP improved over the course of two months. She was then re-evaluated for HCC. Contrast-enhanced CT scan revealed a multiple HCCs in both lobes of the liver with a maximum diameter of 95mm. We assessed the patient as having unresectable HCC, and planned LEN-TACE therapy. Six months after induction of scheduled LEN-TACE, PR (mRECIST) was obtained and conversion surgery was performed 11 months after the initial hospitalization. She obtained once cancer free, but multiple recurrences occurred early postoperatively. Adjuvant lenvatinib was restarted, and she again achieved PR.
Conclusions: Acquired TTP was developed by anti-ADAMTS13 antibody. In this case, we considered the development of tumor-associated antibody. It has been reported that ICI administration can induce TTP, so ICI was considered inappropriate. In the end, LEN-TACE was selected, it provided a good therapeutic effect.

P-29
10093

Hepatocellular Carcinoma with Long Complete Response after Liver and Lung Resections and Lenvatinib

Shohe Kobe, Takao Miwa, Masashi Aiba, Shinji Unome, Tatsunori Hanai, Kenji Imai, Koji Takai, Masahito Shimizu
Department of Gastroenterology/Internal Medicine, Graduate School of Medicine, Gifu University, Japan

Background: Patients with hepatocellular carcinoma (HCC) and lung metastasis are known to have poor prognosis and the treatment for these patients remains an unmet clinical need.
Case presentation: A 39-year-old female presented with an abdominal bloating remaining after childbirth in year X. She had no medical or family history of liver disease, no smoking history, and no alcohol abuse. Physical examination showed a palpable mass under the right costal arch. Magnetic resonance imaging with contrast showed a 117 mm liver tumor in liver segment 6 with enhancement in the arterial phase and reduced uptake in the hepatobiliary phase. Laboratory tests demonstrated elevated alpha-fetoprotein of 3503 ng/mL and protein induced by vitamin K absence or antagonist-II of 71 mAU/mL. There was no evidence of liver disease including viral hepatitis, metabolic dysfunction-associated steatotic liver disease, autoimmune hepatitis, or cirrhosis. Partial hepatectomy of liver segment 6 was performed and the tumor was diagnosed with HCC. She experienced pulmonary metastases resected in years X+4 and X+6, and intrahepatic recurrence in posterior segmentectomy also resected in year X+7. She started lenvatinib 4 mg/day due to high recurrence risk in year X+7 after surgery. Radiofrequency ablation was performed on the remaining early-enhancing tumors in years X+8 and X+10, leading to discontinuation of lenvatinib. Currently, at year X+13, the patient remains in complete remission.
Conclusions: For patients with high-risk HCC and high tolerance to treatment, a multidisciplinary approach combining local therapy and systemic chemotherapy should be considered to improve outcomes.

P-30
10135

Anti-HCV Treatment Using Direct-acting Antivirals during Systemic Immunotherapy for Unresectable Hepatocellular Carcinoma may Contribute to Improving Long-term Prognosis: A Case Report

Wataru Ueno, Shunji Watanabe, Yosuke Otsuka, Rie Goka, Hiroshi Maeda, Kouichi Miura, Naoki Morimoto
Department of Medicine, Division of Gastroenterology, Jichi Medical University, Japan

Patient: 40s, female Present illness: The patient was diagnosed with hepatitis C in 20s. Interferon therapy was performed but was unsuccessful. Two years ago, the patient was diagnosed with unresectable hepatocellular carcinoma with portal vein tumor thrombus (Vp2), leading to a referral to our hospital. With a following curative resection in mind, scheduled LEN-TACE was performed. The best response was PR, but due to a decline in liver function, lenvatinib was discontinued and surgical treatment was abandoned. Instead, immunotherapy with a combination of atezolizumab and bevacizumab (ATZBV) was initiated. The best response was PR and ATZBV treatment is continued, maintaining disease control. Since the persistent infection with hepatitis C virus (HCV) was thought to be one of the causes of impaired liver function, antiviral treatment with sofosbuvir/velpatasvir was administered while continuing ATZBV treatment. While maintaining PR with ATZBV treatment for hepatocellular carcinoma, anti-HCV treatment achieved SVR12, and the liver function has been gradually improving.
Discussion: Maintaining and improving liver function is a crucial factor for long-term prognosis in hepatocellular cancer. In this case, HCV treatment during ATZBV treatment led to an improvement in liver function, allowing for the continued stability of drug therapy and the potential consideration of conversion surgery. Antiviral treatment during liver cancer therapy is expected to improve long-term prognosis by amelioration of liver function. Although there have been reports of rapid growth of HCC after DAA treatment, it may be useful to administer DAAs with careful attention.

P-31
10148

A Case of Fatal Immune-Mediated Myocarditis Following Durvalumab and Tremelimumab Combination Therapy (DT) for Multiple Hepatocellular Carcinomas

Ryo Saito, Junichiro Kumagai, Syuhei Katsumi, Akinori Abe, Tomohiro Haruna, Takeshi Mine, Masamichi Obu, Yu Yoshida, Yoshihiro Koma, Mototsugu Fujimori, Ryosaku Azemoto
Gastroenterology, Kimitsu Chuo Hospital, Chiba, Japan

Background: The use of immune checkpoint inhibitors (ICIs) has increased in recent years. Accordingly, there are more needs to deal with immune-mediated adverse event (imAE) appropriately.
Case: A 73 years old woman with nonalcoholic steatohepatitis-related liver cirrhosis had an incidental multiple hepatocellular carcinomas on contrast-enhanced CT. Her past medical history is myocardial infarction. She was scheduled for treatment with DT. Cardiac function was confirmed to be adequate before initiating treatment. DT was started on Day 1. On Day 8, she developed a fever of 38°C. As the fever persisted, she sought outpatient care on Day 13. Elevated CPK and cardiac biomarkers were observed, leading to a diagnosis of suspected imAE myocarditis. She was urgently admitted on the same day. Treatment with prednisolone at 1 mg/kg/day was initiated on Day 13. CPK levels decreased by Day 17, however, signs of heart failure emerged from Day 18. Infliximab was administered on Day 22, but the patient passed away on Day 23.
Discussion: Although imAE myocarditis is very rare, it has a high mortality rate of approximately 50%. Early diagnosis and prompt high-dose steroid treatment are crucial. Additionally, the risk of imAE myocarditis is associated with ICI combination therapy. And imAE myocarditis is likely to occur within the first 30 days of administration. Conclusion: For patients with pre-existing cardiac conditions undergoing ICI combination therapy, close monitoring for imAE myocarditis is essential. Establishing a system that facilitates early detection and prompt administration of high-dose steroids is vital for effective management of imAE myocarditis.

P-32
10004

Impact of Atezolizumab + Bevacizumab Combination Therapy on Health-related Quality of Life and Relationship with Prognosis in Patients with Advanced Hepatocellular Carcinoma

Masako Shomura[1], Haruka Okabe[1], Maya Sakakibara[1], Emi Sato[2], Koichi Shiraishi[3], Yoshitaka Arase[3], Kota Tsuruya[3], Shunji Hirose[3], Yusuke Mishima[4], Tatehiro Kagawa[3]
[1]Faculty of Nursing, Tokai University School of Medicine, Kanagawa, Japan, [2]Department of Nursing, University of Tokyo Health Science, Tokyo, Japan, [3]Division of Gastroenterology, Department of Internal Medicine, Tokai University School of Medicine, Kanagawa, Japan, [4]Department of Advanced Medical Science, Tokai University Graduate School of Medicine, Kanagawa, Japan

Purpose: To identify factors associated with treatment efficacy, treatment duration, and overall survival (OS) in HCC patients receiving atezolizumab + bevacizumab combination therapy (Atezo+Bev), based on their baseline characteristics, including adverse events (AEs) and Health-related quality of Life (HRQoL) at three months.
Methods: The consecutive HCC patients who received Atezo+Bev from Nov 2020 to Apr 2024 were followed up until Apr 19, 2024, or death. HRQoL was monitored every month by EORTC-QLQ C30. The variables associated with efficacy, OS, and treatment duration were analyzed using multivariate logistic regression and Cox's hazard models.
Results: A total of 64 patients were enrolled: men (83%), aged 70 years or older (50%), Child-Pugh score of 5 (45%), and BCLC C (38%). ORR was 34.9%, with a median treatment duration of 10.8 months and OS of 18.4 months. HRQoL scores of five functional domains, such as general health, physical function (PF), role function, emotional function, and cognitive function (CF), significantly worsened during the first three months. Extrahepatic invasion (OR 0.19, 95% CI: 0.05-0.78) and TNM stage IV (OR 0.25, 95%CI: 0.08-0.80) were associated with lower ORR. Grade 2/3 skin toxicity (OR: 6.67, 95%CI: 1.17-38.46) and CF≥80 (OR 9.19,95%CI: 1.80-46.79) at three months contributed to higher ORR. Hypoalbuminemia Grade 2 or higher [HR 3.80, 95%CI:1.48-9.77] at three months was a poor prognosis, and PF≥80 [HR 0.45, 95%CI:0.21-0.99] showed a better OS.
Conclusion: Worsened HRQoL and adverse events affect its effectiveness, so it is essential to maintain HRQoL and prevent AEs through patient education and continuous multidisciplinary management.

P-33
10038

Cytokine Analysis as a Predictive Biomarker of Response to Treatment with Atezolizumab and Bevacizumab in Advanced Hepatocellular Carcinoma

Satoshi Kobayashi, Taito Fukushima, Kazumasa Shiraishi, Masato Enomoto, Tomomi Hamaguchi, Yasutsugu Asai, Yuichiro Tozuka, Makoto Ueno
Department of Gastroenterology, Kanagawa Cancer Center, Japan

Background: Atezolizumab plus bevacizumab (ATZ+BEV) has been a standard of treatment for patients with advanced hepatocellular carcinoma (aHCC). Although its efficacy, predictive biomarker of response to the treatment was still unestablished.
Methods: We prospectively enrolled 28 patients with aHCC who would initiate ATZ+BEV. We collected plasma samples from them before the initiation of ATZ+BEV and after progression against it. We analyzed seventeen cytokines related to angiogenesis and immune system in each sample: PIGF, HGF, Ang2, s-Neuropilin, OPN, serum(s)-VEGFR1/2/3, VEGF-A/D, TSP2, TIMP1, s-ICAM1, s-VCAM1, IL-6/8, and IFN-γ. We evaluated the association between the level of these cytokines and their prognosis.
Results: The initial levels of the cytokines were quite different in each patient. Therefore, we defined the outlier level in each cytokine as "high". None of the cytokines was not predictive for the radiological response, but high level of s-Neuropilin (>600,000 pg/mL) and VEGF-D (>800 pg/mL) were associated to poor progression-free survival (p = 0.005 and 0.041, respectively). Regarding to the change in cytokine level between before and after the treatment, the decrease of VEGF-A/-D and the increase of Ang2 seemed poor prognostic factors for post progression-free survival (p = 0.120, 0.120 and 0.070, respectively).
Conclusion: s-Neuropilin and VEGF-D is a predictive biomarker of response to ATZ+BEV in patients with aHCC. When progressed against ATZ+BEV, patients whose angiogenesis in the tumor was dependent on VEGF-VEGFR signaling, not on Ang2-Tie2 signaling, had a better prognosis after failure to ATZ+BEV.

P-34
10055

Pretreatment Predictors of Response to Combination Therapy with Atezolizumab/Bevacizumab in Advanced Stage Hepatocellular Carcinoma

Norikazu Tanabe[1,2], Issei Saeki[2], Maho Egusa[2], Tsuyoshi Fujioka[2], Takahiro Yamasaki[1,3], Taro Takami[2]
[1]Yamaguchi University Hospital Division of Laboratory, Ube, Japan, [2] Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Ube, Japan, [3]Department of Oncology and Laboratory Medicine, Yamaguchi University Graduate School of Medicine, Ube, Japan

Background: We previously reported that tumor markers should be focused on as early predictors of response to combination therapy with atezolizumab/bevacizumab (atezo/bev) for unresectable hepatocellular carcinoma (HCC). However, the pretreatment predictors remain unclear. This study aimed to identify such predictors in BCLC stage C HCC patients treated with atezo/bev in our hospital.
Methods: Forty-four patients with BCLC stage C HCC patients treated with atezo/bev from October 2020 to May 2024 were included. We analyzed the pretreatment factors that contributed to the response.
Results: The median age was 74 years, and 37 males (84.1%) were included in this study. The mALBI grades were 1/2a/2b/3: 13 (29.5%)/6 (13.6%)/22 (50.0%)/3 (6.8%). 37 (84.1%) patients had intrahepatic lesions, 18 (40.9%) patients had macrovascular invasion, 18 (40.9%) patients had metastasis to other organs, and 15 (34.1%) patients had lymph node metastasis (LNM). The median AFP and DCP levels were 92.3 ng/mL and 494.9 mAU/mL, respectively. Atezo/bev was administered as first-line therapy in 34 patients (77.3%). The best response rates were CR/PR/SD/PD/NE: 0/19 (43.2%)/15 (34.1%)/9 (20.5%)/1 (2.3%). Multivariate analysis identified the presence of LNM as a contributing factor to the response (odds ratio, 5.5; p=0.049). The response rate was 66.7% with LNM vs. 31.0% without LNM, p=0.023; progression-free survival was 9.7 vs. 7.1 months, p=0.151; and overall survival was 22.4 vs. 18.5 months, p=0.060, with a trend toward better survival in patients with LNM.
Conclusions: Advanced stage HCC with LNM at therapy initiation may respond to atezo/bev therapy.

P-35
10141

Clinical Significance of Oncological Resectability Criteria in Patients Treated with Atezolizumab and Bevacizumab

Yutaka Yasui, Kaoru Tsuchiya, Mina Taguchi, Yudai Yamazaki, Naoki Uchihara, Yuki Tanaka, Shohei Kimura, Junko Yagita, Taisei Keitoku, Risa Okada, Mayu Higuchi, Kenta Takaura, Shohei Tanaka, Chiaki Maeyashiki, Nobuharu Tamaki, Hiroyuki Nakanishi, Yuka Takahashi, Namiki Izumi, Masayuki Kurosaki
Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Japan

Background and Aims: Oncological resectability criteria have recently been proposed for HCC as a common language for both surgeons and hepatologists. This study examined the clinical significance of this classification in patients who received systemic treatment.
Methods: We conducted a retrospective study enrolling 151 consecutive HCC patients treated with atezolizumab and bevacizumab. Overall survival (OS) and progression-free survival (PFS) were analyzed based on oncological resectability criteria reported by Akahoshi et al. (Liver Cancer, 2024).
Results: Using the oncological resectability criteria, patients were evaluated as resectable (R): 9 patients, borderline resectable 1 (BR1): 53 patients, and borderline resectable 2 (BR2): 89 patients. The reasons for BR1 were vascular invasion (vp2-3 or B2-3) in 25 patients and localized extrahepatic spread in 3 patients. Similarly, the reasons for BR2 were vascular invasion (vp4) in 8 patients and distant metastasis in 35 patients. The objective response rate was 24% for BR1 and 22% for BR2 (p=0.83), and the disease control rate was 70% for BR1 and 80% for BR2 (p=0.22). Four patients who achieved curative conversion resection were BR1 patients, while five BR2 patients achieved complete response with pharmacotherapy alone or with additional locoregional therapy. Conversion/CR patients had a significantly better prognosis than others (p=0.01). Neither OS nor PFS were significantly different between BR1 and BR2.
Conclusions: Patients achieving conversion resection or CR in BR1 and BR2 groups showed significantly prolonged prognosis. No significant differences were observed in response rate, OS, or PFS between BR1 and BR2 in patients where pharmacotherapy was introduced.

P-36
10155

Outcomes of Atezolizumab Plus Bevacizumab (Atezo/Bev) Therapy for Hepatocellular Carcinoma (HCC) without Macroscopic Vascular Invasion (MVI) or Extrahepatic Spread (EHS) ~ Focus on Tumor Factors

Michihisa Moriguchi, Seita Kataoka, Yusa Seko, Kanji Yamaguchi, Yoshito Itoh
Molecular Gastroenterology and Hepatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Background: Few reports have examined the outcomes of Atezo/Bev therapy for HCC without MVI or EHS, focusing on factors such as number of tumors, maximum tumor diameter (MTD), and tumor burden, and the purpose of this study is to analyze these aspects.
Methods: Ninety-three HCC patients without MVI or EHS who underwent imaging evaluation treated with Atezo/Bev were included, and retrospectively analyzed for objective response rate (ORR), disease control rate (DCR), progression free survival (PFS) based on RECIST v1.1.
Results: Patient characteristics were as follows: age >75 years; 60.2%, male; 84.9%, PS 0; 73.1%, Child-Pugh 5; 61.3%, Etiology (non-B non-C); 64.5%, MTD; 30 (10.5-174.5) mm, >70 mm; 14.0%, number of tumors >5; 55.9%, >10; 19.4%, up-to-11 out; 30.1%, AFP>400 ng/ml; 18.3%, Atezo/Bev introduction as 1st line treatment; 58.1%, history of trans-arterial chemoembolization; 63.4%. Median overall survival was 21.1 months, the ORR and DCR were 31.2 and 75.3%, respectively. No significant factors contributing to ORR were extracted, and only AFP (<400 ng/ml vs. 400 ng/ml<) was extracted as a significant factor for DCR by multivariate analysis (p=0.018, odds ratio=0.243). As significant factors contributing to PFS, multivariate analysis showed that MTD (<70 mm vs. 70 mm<; p=0.031, hazard ratio (HR)=0.395), number of tumors (<9 vs. 10<; p<0.001, HR=3.086), AFP (<400 ng/ml vs. 400 ng/ml<; p=0.001, HR=2.680) were extracted, but up-to-11 criteria was not a significant factor.
Conclusion: The efficacy of Atezo/Bev therapy for HCC without MVI or EHS may depend on factors such as MTD, number of tumors, and AFP value.

P-37
10161

CyTOF Reveals Platelet Subtype Changes Predicting the Efficacy of Combined Immunotherapy and Targeted Therapy in Liver Cancer

Junfeng Lu[1,3], Dan Liu[1], Lilin Wang[1], Wubuli Aishan Maimaitijiang[3], Yuefeng Shang[2], Sunjun Zheng[1], Wenjing Wang[2]
[1]Beijing Youan Hospital, Capital Medical University, [2]Beijing Institute of Hepatology, Beijing You An Hospital, Capital Medical University, [3]Hotan District Infectious Disease Specialist Hospital, China

Background: Immune checkpoint inhibitors(ICIs) combined with anti-angiogenic agents (AAs) angiogenesis inhibitors are currently the first-line treatment for liver cancer, but some patients still experience poor efficacy. Platelets are closely related to liver cancer due to their impact on angiogenesis and the tumor immune microenvironment. We aimed to explore the function and changes of platelets in patients with liver cancer adopting ICIs and AAs therapy in this study.
Method: We used CyTOF to detect surface proteins on platelets in the plasma of 23 patients with liver cancer before and after combination therapy and 10 healthy donors, analyzed the differences according to treatment efficacy.
Result: The subpopulations of CD107a-positive and CD62P-positive platelets were reduced in liver cancer patients compared to healthy donors. In the group with progressive disease, the CD29-positive platelet subpopulation increased compared to other groups, and this subpopulation decreased with tumor remission and increased with tumor progression.
Conclusions: Our results demonstrate the heterogeneity of platelets in liver cancer patients, suggesting that the CD29-positive platelet subpopulation may serve as a biomarker for predicting the efficacy of combination therapy in liver cancer. CD29-positive platelets could also be a potential therapeutic target in future research.

P-38
10059

Predictive Factors for Objective Response Rate in Patients with Unresectable Hepatocellular Carcinoma Treated with Durvalumab Plus Tremelimumab Therapy

Yuki Shirane, Yasutoshi Fujii, Atsushi Ono, Shinsuke Uchikawa, Hatsue Fujino, Eisuke Murakami , Daiki Miki , Tomokazu Kawaoka , Masataka Tsuge, Shiro Oka
Department of Gastroenterology, Hiroshima University Hospital, Hiroshima, Japan

Background: Durvalumab plus Tremelimumab combination therapy (STRIDE regimen) is a new first-line option for unresectable hepatocellular carcinoma (uHCC), but little real-world data is available to determine which patients are most likely to respond. In this study, we analyzed overall therapeutic outcomes of the first experience with the STRIDE regimen for uHCC. In particular, we focused on identifying factors associated with cases that had a favorable response.
Methods: This study retrospectively evaluated 48 patients with uHCC who were treated with STRIDE regimen at Hiroshima University Hospital between April 2023 and December 2023. The end of follow-up was March 2024 and the median follow-up period was 8.8 months. The primary endpoint of the study was objective response rate (ORR).
Results: Under both RECIST and mRECIST, ORR was significantly higher in the 1st line group compared to the later line group (RECIST: $p = 0.0001$, mRECIST: $p < 0.0001$). And the 1st line group had longer PFS than the later line group ($p = 0.007$). We focused the analysis of factors contributing to response on the 1st line group because response was exclusively observed in that group. Multivariate logistic regression analysis identified high tumor-to-liver ratio of the SUVmax (TLR) on baseline FDG-PET as an independent factor associated with PR (odds ratio 2.3 95% CI = 0.87-6.0, $p = 0.044$). TLRs were significantly higher in poorly and undifferentiated uHCC.
Conclusions: The STRIDE regimen may be beneficial for systemic therapy-naive uHCC patients. High TLR on baseline FDG-PET could be a potentially useful biomarker for predicting response.

Poster Session

P-39
10062

Efficacy and Safety of Durvalumab plus Tremelimumab for Advanced Hepatocellular Carcinoma with Esophageal Varices

Naoshi Odagiri[1], Jumpei Okamura[2], Yoshimi Yukawa-Muto[1], Kohei Kotani[1], Hiroyuki Motoyama[1], Ritsuzo Kozuka[1], Hideki Fujii[1], Sawako Uchida-Kobayashi[1], Masaru Eomoto[1], Hideyuki Tamai[2], Norifumi Kawada[1]
[1]Department of Hepatology, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan, [2]Department of Hepatology, Wakayama Rosai Hospital, Wakayama, Japan

Background: In cases of unresectable hepatocellular carcinoma (HCC) with varices, durvalumab plus tremelimumab (Dur+Tre) is often chosen as systemic chemotherapy to avoid the risk of variceal bleeding. We aimed to evaluate the efficacy and safety of Dur+Tre therapy for HCC with esophageal varices in a clinical setting.
Methods: A total of 20 patients with advanced HCC who received Dur+Tre therapy at our institutions between March 2023 and July 2024 were enrolled. Tumor responses, overall survival (OS), progression-free survival (PFS), and adverse events (AE) were evaluated.
Results: The median age was 71 years and 16 (80.0%) patients were male. 1/9/10 patients were classified as BCLC stage A/B/C. 7 patients had esophageal varices (5 and 2 patients with F1 and F2, respectively) and 5 patients had a history of treatment for varices. Median ALBI score was higher in patients with varices (-2.59 vs -1.83, p=0.024). A lower tendency of disease control rate was found in patients with varices (0.0 vs 46.2%, p=0.07). After a median follow-up of 6.0 months, median OS (2.7 [1.2-NA] vs NA [5.9-NA] months, p=0.002) and PFS (1.4 [0.9-NA] vs 5.3 [1.5-NA] months, p=0.001) were shorter in patients with varices. While there were no cases of variceal bleeding, grade 3-5 AEs were found more frequently in patients with varices (85.7 vs 23.1%, p=0.017). The proportion of patients who underwent subsequent treatments was lower in the group with varices (14.3 vs 75.0%, p=0.020).
Conclusion: While Dur+Tre can be used in patients with varices at risk of bleeding, the therapeutic benefit may be limited.

P-40
10069

Effective Monitoring of Durvlumab plus Tremelimumab Therapy Using Tumor Marker

Issei Saeki[1,11], Shigeo Shimose[2,11], Tetsu Tomonari[3,11], Takanori Ito[4,11], Joji Tani[5,11], Yasuto Takeuchi[6,11], Takeshi Hatanaka[7,11], Kyo Sasaki[8,11], Sohji Nishina[8], Motoyuki Otsuka[9], Hideki Kobara[5], Takumi Kawaguchi[2,9], Takahiro Yamasaki[9], Taro Takami[1]
[1]Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Yamaguchi, [2]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, [3]Department of Gastroenterology and Oncology, Institute of Biomedical Sciences, Tokushima University Graduate School of Medicine, Tokushima, [4]Department of Gastroenterology and Hepatology, Nagoya University Graduate School of Medicine, [5]Department of Gastroenterology and Neurology, Kagawa University, Faculty of Medicine, Kagawa, [6]Department of Regenerative Medicine, Center for Innovative Clinical Medicine, Okayama University Hospital, Okayama, [7]Department of Gastroenterology, Gunma Saiseikai Maebashi Hospital, Maebashi, [8]Department of Gastroenterology and Hepatology, Kawasaki Medical School, Kurashiki, [9]Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, [10]Department of Oncology and Laboratory Medicine, Yamaguchi University Graduate School of Medicine, Yamaguchi, [11]Hepatology InVestigator Experts in Japan (HIVE-J) Study Group, Japan

Background: In immunotherapy for hepatocellular carcinoma (HCC), it is important to sequence appropriately in refractory cases. Tumor markers have been used as biomarkers to predict response to systemic therapy, and the aim of this study was to evaluate the efficacy of durvalumab plus tremelimumab (Durva/Treme) therapy for HCC.
Methods: 110 patients with HCC treated with Durva/Treme therapy were retrospectively enrolled from a multicenter.
Results: Objective response rate (ORR) and disease control rate (DCR) were 15.5% and 53.6%, respectively. Median progression-free survival (mPFS) was 3.0 months. Predictive factors contributing to response were evaluated at two points: pre-induction and post-induction (4 weeks). In the analysis of pre-induction factors, only baseline AFP level >400 ng/mL (odds ratio 3.497, p=0.029) was identified as a predictor of OR by multivariate analysis. Patients with AFP >400 ng/mL had a significantly higher ORR than those with AFP <400 ng/mL (28.2 vs. 8.5%, p=0.011), but no significant difference in PFS. In addition, changes in tumor markers were included in the post-treatment analysis, and AFP/DCP response was defined as >10% decrease from baseline. Both AFP response (odds ratio 6.023, p=0.042) and DCP response (odds ratio 11.657, p=0.006) were extracted as independent factors for OR prediction. Patients with AFP/DCP response had significantly longer PFS than those without response.
Conclusion: AFP and DCP are useful for monitoring response in patients with HCC treated with Durva/Treme therapy.

Poster Session

P-41
10089

Efficacy and Safety of Immunotherapy for Real-World Elderly Patients with Unresectable Hepatocellular Carcinoma in Japan

Shun Kaneko[1,13], Yasuhiro Asahina[1,2,13], Miyako Murakwa[1,13], Shunsuke Ueyama[3,13], Hideki Watanabe[4,13], Chiaki Maeyashiki[5,13], Akiko Kusano-Kitazume[6,13], Ayako Sato[7,13], Taro Watabe[8,13], Kozue Uchidate[9,13], Hiroki Ueda[10,13], Keiichi Akahoshi[10,13], Tsubasa Nobusawa[1,13], Taro Shimizu[1,13], Jun Tsuchiya[1,13], Masato Miyoshi[1,13], Fukiko Kawai-Kitahata[1,13], Mina Nakagawa[1,11,13], Sei Kakinuma[1,12,13], Ryuichi Okamoto[1,13]
[1]Department of Gastroenterology and Hepatology, Tokyo Medical and Dental University, Tokyo, [2]Department of Liver Disease Control, Tokyo Medical and Dental University, Tokyo., [3]Department of Gastroenterology and Hepatology, Tsuchiura Kyodo General Hospital, Ibaraki, [4]Department of Gastroenterology and Hepatology, Yokosuka Kyosai Hospital, Kanagawa, [5]Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Tokyo, [6]Department of Gastroenterology and Hepatology, Tokyo Metropolitan Tama Medical Center, Tokyo, [7]Department of Gastroenterology and Hepatology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, [8]Department of Gastroenterology and Hepatology, Ome Medical Center, Tokyo, [9]Department of Gastroenterology and Hepatology, JA Toride Medical Center, Ibaraki, [10]Department of Hepatobiliary and Pancreatic Surgery, Tokyo Medical and Dental University, Tokyo, [11]Institute of Education, Tokyo Medical and Dental University, Tokyo, [12]Department of Clinical and Diagnostic Laboratory Science, Tokyo Medical and Dental University, Tokyo, [13]Ochanomizu Liver Conference Study Group, Japan

Background/Aim: The global population, including patients with hepatocellular carcinoma (HCC), is aging. This study evaluated the efficacy and safety of immunotherapy and identified prognostic factors in elderly HCC patients, reflecting a real world population.
Methods: A total of 286 patients (242 aged ≥65) treated with atezolizumab + bevacizumab or durvalumab + tremelimumab as first line therapy from November 2020 to January 2024 at 16 hospitals were included. Patients were divided into three age groups: under elderly (UE; ≤64 years), early elderly (EE; 65-74 years), and late elderly (LE; ≥75 years).
Results: The proportion of patients was 44 (15.4%), 125 (43.7%), and 117 (40.9%) in UE, EE, and LE, respectively, with any adverse events occurring in 45.4%, 38.4%, and 46.1% of patients. UE patients had higher AFP levels, higher ALT levels, and a lower disease control rate (59.1% vs. 77.7%) compared to EE and LE patients. LE patients had a lower albumin-bilirubin (ALBI) score (-2.478 vs. -2.296) and more proteinuria (21.3%). Multivariate analysis identified the ALBI score as an independent prognostic factor (HR 2.005, 95% CI 1.44–2.790, P < 0.001). The modified ALBI grade showed the highest discrimination for 1 and 2 year survival prediction. Among patients with ALBI 1/2a, there was no significant difference in overall survival across age groups (median months: 22.2, 19.7, 30.4, P=0.40). The Fine-Gray competing risk model found no significant difference in liver-related and other deaths (P=0.34).
Conclusion: Immunotherapy for elderly HCC patients should consider liver function and overall condition, with ALBI score evaluation crucial for improving prognosis.

P-42
10110

Treatment Efficacy in Durvalumab plus Tremelimumab Therapy for Unresectable Hepatocellular Carcinoma with Previous Immune Check Point Inhibitor

Nami Mori[1], Nobuharu Tamaki[2], Masayuki Kurosaki[2]
[1] Department of Gastroenterology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital, Hiroshima , [2]Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Tokyo, Japan

Background: The optimal positioning of durvalumab plus tremelimumab (DT) and atezolizumab plus bevacizumab (AB) as treatment strategies for uHCC to maximize therapeutic efficacy remains uncertain. Therefore, we assessed the efficacy of DT therapy in a nationwide, multicenter study.
Methods: We enrolled 104 uHCC cases. Eighty-five cases without missing imaging or blood data and excluding Child-Pugh class C were analyzed (median age 75 years; Child-Pugh class A: B= 59:26; BCLC stage A: B= 1:39:45, median observation period 5.4 months). Treatment efficacy was evaluated at eight weeks using RECIST 1.1.
Results: Treatment settings were first line (1st): later line (later) = 16:69 cases, with 58 cases having prior AB. Overall, the ORR was 18% and the DCR was 42%. ORR in 1st, later without prior AB, and later with prior AB were 44%, 55%, and 5%, respectively. DCR was 75%, 91%, and 26%, respectively. The group with prior AB therapy showed significantly lower ORR and DCR (ORR: p&It;0.001, DCR: p&It;0.001). Median PFS overall was 2.8 months; for the 1st, later without prior AB and later with prior AB were 5.2 months, not reached, and 2.9 months, respectively. Multivariable analysis using 1st as a reference demonstrated the adjusted HR (95% CI) for PFS was 0.28 (0.06-1.4, p = 0.1) for later without AB and 2.35 (1.1-5.1, p = 0.03) for later with prior AB. PFS was significantly shorter than prior AB.
Conclusion: The effect of DT after AB was limited. Therefore, previous treatment history should be considered when initiating DT.

P-43
10007

Surgical Outcomes of Combined Hepatocellular-Cholangiocarcinoma in Comparison to Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma: A Propensity-Score Matched Analysis

Hae Won Lee, Yeshong Park, Jinju Kim, MeeYoung Kang, Boram Lee, Jai Young Cho, Yoo-Seok Yoon, Ho-Seong Han
Department of Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

Introduction: Combined hepatocellular-cholangiocarcinoma (HCC-CCA) is a rare primary liver malignancy with pathological features of both hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (CCA). The aim of this study was to compare the clinical characteristics and survival outcomes of HCC-CCA in comparison to HCC and CCA.
Method: All consecutive liver resections for primary liver cancer at Seoul National University Bundang Hospital from January 2003 to December 2022 were included for analysis. Propensity-score matching (PSM) was performed through two sequential matching processes.
Results: Among 1479 patients, 1343 (90.8%) underwent surgery for HCC, 78 (5.8%) for HCC-CCA, and 58 (3.9%) for CCA. In the CCA group, open surgery and major liver resection were more frequently performed. HCC-CCA was associated with larger tumor size, higher T stage, higher microvascular invasion rate, and frequent serosal involvement. After PSM, 164 (HCC 82, HCC-CCA 41, CCA 41) patients were successfully matched. Five-year recurrence free survival rates were significantly worse in HCC-CCA and CCA compared to HCC (HCC 51.2% vs. HCC-CCA 31.6% vs. CCA 34.4%, P = 0.014). Five-year overall survival rates showed no statistically significant difference (HCC 81.6% vs. HCC-CCA 63.4% vs. CCA 64.6%, P = 0.120).
Conclusions: Although HCC-CCA and HCC are similar in patient demographics and underlying liver condition, the recurrence pattern of HCC-CCA resembles that of CCA. This might be due to aggressive pathological characteristics including larger tumor size, advanced T stage, and higher microvascular invasion rate.

P-44
10030

Short- and Long-term Outcomes of Laparoscopic Liver Resection for Non-alcoholic Fatty Liver Disease-associated Hepatocellular Carcinoma

Yukihiro Watanabe, Masayasu Aikawa, Yoshiki Murase, Kenichiro Takase, Yuichiro Watanabe, Katsuya Okada, Yasumitsu Hirano, Shinichi Sakuramoto, Kojun Okamoto, Isamu Koyama
Saitama Medical University International Medical Center, Gastroenterological Surgery, Saitama, Japan

Background: We compared the recurrence-free survival (RFS), overall survival (OS), and safety of laparoscopic liver resection (LLR) between non-alcoholic fatty liver disease (NAFLD) and non-NAFLD hepatocellular carcinoma (HCC) patients.
Methods: Patients with HCC (n = 349) were divided into four groups based on the HCC etiology (NAFLD [n = 71], hepatitis B [n = 27], hepatitis C [n = 187], alcohol/autoimmune hepatitis [AIH] [n = 64]). RFS and OS were assessed by multivariate analysis after adjustment for clinicopathological variables. A subgroup analysis was performed based on the presence (n = 248) or absence (n = 101) of cirrhosis.
Results: Compared with the NAFLD group, the hazard ratios (95% confidence intervals) for RFS in the hepatitis B, hepatitis C, and alcohol/AIH groups were 0.49 (0.22-1.09), 0.90 (0.54-1.48), and 1.08 (0.60-1.94), respectively. For OS, the values were 0.28 (0.09-0.84), 0.52 (0.28-0.95), and 0.59 (0.27-1.30), respectively. With cirrhosis, NAFLD was associated with worse OS than hepatitis C (P=0.010). Without cirrhosis, NAFLD had significantly more complications (P=0.034), but comparable survival than others.
Discussion: Patients with NAFLD-HCC have some disadvantages after LLR. In patients with cirrhosis, LLR is safe, but survival is poor. In patients without cirrhosis, the complication risk is high.

P-45
10054

Significance of Repeated Laparoscopic Liver Resection for Recurrent HCC after Curative Treatment

Yuji Iimuro[1], Atsushi Takano[1], Kenji Amemiya[2], Yosuke Hirotsu[2], Hitoshi Mochizuki[2,3], Shuntaro Obi[3,4], Masao Omata[3,5]
[1]Department of Surgery, Yamanashi Central Hospital, Yamanashi, Japan, [2]Genome Analysis Center, Yamanashi Central Hospital, Yamanashi, Japan, [3]Department of Medicine, Yamanashi Central Hospital, Yamanashi, Japan, [4]Department of Medicine, Teikyo University Chiba Medical Center, Chiba, Japan, [5]The University of Tokyo, Tokyo, Japan

Hepatocellular carcinoma often recurs after curative resection, and repeated liver resection is one of the treatment choices in case of good liver function. We investigated the safety and oncologic significance of repeated laparoscopic liver resection for recurrent HCC.
Methods: Among 200 HCC patients who received curative resection in our hospital, 30 underwent re-resection for recurrence. Genomic differentiation between intrahepatic metastasis (IM) and multicentric occurrence (MO) comparing primary and recurrent tumors was performed, employing an in-house target sequence panel with a next-generation sequencer. Laparoscopic re-resection was performed in 25 out of 30 patients, and its safety was also analyzed.
Results: Among the 30 cases that underwent resection for recurrent lesions after initial treatment, there were 17 MO recurrences and 13 cases of IM recurrence. There was no significant difference in recurrence-free survival (RFS) between MO and IM recurrence after initial liver resection. Meanwhile, RFS after the second resection was significantly better in MO cases ($p<0.05$). Overall survival (OS) was significantly better in the MO recurrence group ($p<0.05$), with 13 out of 17 cases maintaining a relatively long-term tumor-free state after re-resection. On the other hand, among the 13 cases of IM recurrence, 10 cases experienced repeated recurrence after liver resection. No major postoperative complications were observed in 25 cases who received laparoscopic liver re-resection, and hospital stay was comparable with that in initial resection.
Conclusion: Repeated laparoscopic liver resection is a safe and effective treatment choice for recurrent HCC. In particular, treatment efficacy can be obtained in recurrent MO cases.

P-46
10057

Attenuation of Hepatic Ischemia-reperfusion Injury Associated with Liver Transplantation by Curcumin in Rodents via Anti-inflammatory Action

Ekta Yadav
Sam Higginbottom University of Agriculture Technology and Sciences, Allahabad, India

Background: Curcumin is a natural polyphenol obtained from Curcuma longa having significant potential against oxidative stress, inflammation, cancer and hepatic toxicity. In present study we focused on the protective effect of curcumin on hepatic ischemia-reperfusion injury by using in vitro and in vivo evaluation.
Methods: Male Sprague-Dawley rats were divided into five groups and administered with curcumin by an intraperitoneal route at three dose levels, i.e., 5, 10 and 20 mg/kg, for 14 days and subjected to liver transplant. RAW 264.7 cells under hypoxia/reoxygenation model were used and treated with curcumin at 1, 10, and 20 M. Curcumin potential against hepatic ischemia-reperfusion injury was estimated by determining liver enzymes, cytokine status, hepatocyte apoptosis level and TUNEL (Terminal deoxynucleotidyl transferase dUTP nick-end labeling), neutrophil and pro-inflammatory cytokines protein, and mRNA expression were detected.
Results: Results of in vivo study revealed that pathological liver alterations, level of serum aminotransferase as well as proinflammatory cytokines (IL-1, IL-18 and TNF-alpha) were significantly decreased by curcumin in a dose-dependent manner. Moreover, reduced protein expression levels of TLR-4, p-IB, p-IKK, p-IKK, p-IKK, NLRP3, p-P65MyD88, TNF-alpha, cleaved caspase-1, IL-1, IL-6 and IL-18 which are basically associated with TLR-4/NF-B/NLRP3 inflammatory signaling pathway was observed in rats with liver transplantation. Dose-dependent inhibition of protein expression associated with TLR-4/NF-B/NLRP3 inflammatory pathway in the RAW264.7 cells with hypoxia/reoxygenation model in curcumin-treated group was observed.
Conclusion: Curcumin exerts an anti-inflammatory effect in hepatic ischemia-reperfusion injury in liver transplantation by regulating the TLR-4/NF-B/NLRP3 inflammatory signaling pathway.

P-47
10082

Current Status of Tumor Ablation in Japan and the Japan Academy of Tumor Ablation (JATA)

Shuichiro Shiina[1], Ryosuke Tateishi[2], Nobuhiro Fukunari[3], Tatsuya Yamashita[2], Yasunori Minami[4], Haruyuki Takaki[5], Kazuhiro Nouso[6], Yuko Takami[7]
[1]Department of Gastroenterology, Juntendo University, Tokyo, Japan, [2]Department of Gastroenterology, The University of Tokyo, Tokyo, Japan, [3]Department of Thyroid Center, Showa University Northern Yokohama Hospital, [4]Department of Gastroenterology, Kindai University Hospital, [5]Department of Radiology, Hyogo College of Medicine, [6]Department of Gastroenterology, The Okayama City Hospital, [7]Department of Hepato Biliary Pancreatic Surgery, National Hospital Organization Kyushu Medical Center, Japan

SURF trial demonstrated that liver resection is not superior to RFA in terms of OS and RFS. Conducted as a RCT across 49 institutions in Japan, SURF trial enrolled patients with HCC over six years starting in 2009, with follow-ups extending five years post-enrollment. Reflecting these findings and other studies, Japanese Clinical Practice Guidelines for HCC now treat resection and ablation as equivalent options for patients with up to three tumors, each 3 cm or smaller.Regarding colorectal liver metastasis, a multicenter RCT in Europe (COLLISION trial) found no significant difference in OS and RFS between ablation and resection, though ablation was associated with lower morbidity and mortality. As of September 2022, public health insurance in Japan covers RFA for lung, renal, and bone and soft tissue tumors, with coverage extending to breast cancer as of December 2023.JATA was established to enhance cooperation among its members and related institutions, aiming for the safe and effective performance of all types of ablations, including RFA, microwave ablation, and cryoablation, across various body areas such as the lung, thyroid, kidney, adrenal gland, breast, bone, soft tissue, and liver. Japan, the originator of techniques like percutaneous ethanol injection and microwave ablation, continues to lead globally in this field. JATA invites participation to advance clinical experience, research, and training for future generations, contributing to the development of ablation techniques.Given its curative potential, minimally invasive nature, repeatability for recurrences, and cost-effectiveness, ablation is expected to play a growing role in Japan's aging population.

P-127
10129

Efficacy of HAIC with 3D-CRT for Unresectable Advanced Hepatocellular Carcinoma Complicated by Major Vascular Tumor Thrombosis

Joji Tani, Rie Yano, Kei Takuma, Mai Nakahara, Kyoko Oura, Tomoko Tadokoro, Koji Fujita, Asahiro Morishita, Hideki Kobara
Department of Gastroenterology and Neurology, Kagawa University, Faculty of Medicine, Japan

Aims: HCC complicated by macrovascular invasion (MVI) is associated with poor prognosis and has no established standard treatment. The aim of this study was to retrospectively evaluate the response rate, survival outcome, and adverse effects of hepatic artery infusion chemotherapy (HAIC) combined with three-dimensional conformal radiotherapy (3DCRT) for intrahepatic tumor in patients with advanced HCC complicated by MVI.
Methods: 51 patients with advanced HCC complicated by MVI with sufficient residual hepatic function, regardless of the degree of disease progression were treated with this combination therapy modality from 2009 to 2023. HAIC consisted of cisplatin in lipiodol emulsion combined with 5-fluorouracil (NewFP). In principle, 3DCRT was given at a total dose of 50 Gy.
Results: Of the 51 patients treated with NewFP with 3DCRT for MVI, 5, 28 and 10 patients had CR, PR, and SD, respectively. The treatment effect on MVI only was CR and PR in 20 and 22 cases, respectively. ORR was 64.7%, and DCR was 84.3%. The median survival time was 12.9 months for all 49 cases. The MST for treatment response to MVI was 2.2 months for SD+PD patients and 20.4 months for CR+PR patients (p&It;0.001).The MST was 7.2 months for patients treated by NewFP with 3DCRT for MVI and 28.9 months for those treated with systemic therapy after NewFP with 3DCRT for MVI (p=0.0123).
Conclusions: NewFP with 3DCRT is demonstrated to be a safe and effective treatment option for patients with unresectable advanced HCC complicated by MVI.

P-48
10008

Clinical Significance of Biliary Invasion at Diagnosis in Barcelona Clinic Liver Cancer Stage B-C Hepatocellular Carcinoma: A Nationwide Cohort Analysis in South Korea

Sunmin Park, Chai Hong Rim, Won Sup Yoon

Korea University Ansan Hospital, Korea

Background: This study investigated the impact of biliary involvement in patients with Barcelona Clinic Liver Cancer stage B-C hepatocellular carcinoma.
Methods: The Korean Liver Cancer Study Group randomly extracted data of patients with hepatocellular carcinoma enrolled in the Korean Central Cancer Registry between 2011 and 2016. 4077 patients with and without bile duct invasion were matched 1:2 based on clinical and tumor characteristics to form a propensity score-matched cohort.
Results: Among 4077 patients, 4.0% showed biliary invasion at diagnosis. One- and two-year overall survival rates were 41.2% and 29.1% for patients with invasion, compared to 54% and 40.9% for those without ($p<0.0001$). Corresponding cancer-specific survival rates at one and two years were 43.4% and 30.7% for patients with invasion, and 56.6% and 44% for those without ($p< 0.0001$). Although biliary invasion significantly affected survival rates in univariate analysis, it was not significant in multivariate analysis for overall ($p=0.153$) and cancer-specific ($p=0.198$) survival rates. Propensity score matching included 165 patients with biliary invasion and 330 without. In this cohort, biliary invasion did not significantly affect overall ($p=0.603$) or cancer-specific ($p=0.960$) survival rates. Multivariate analysis identified significant factors: alpha-fetoprotein levels, Child-Pugh class, tumor singularity, size, portal invasion, lymph node, and distant metastases.
Conclusion: Biliary invasion at diagnosis in patients with BCLC B-C does not affect overall or cancer-specific survival rates; however, other prognostic factors associated with biliary invasion could have a greater impact.

P-49
10020

Clinical Characteristics and Prognosis of Hepatocellular Carcinoma Patients without Liver Fibrosis

Fujimasa Tada[1], Hideko Ohama[1], Atsushi Hiraoka[1], Tomoyuki Ninomiya[1], Yoshiko Nakamura[2], Masashi Hirooka[2], Yoichi Hiasa[2]
[1]Gastroenterology Center, Ehime Prefectural Central Hospital, Matsuyama, Japan, [2]Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Toon, Japan

Background: Recently, proportion of non-hepatitis-related hepatocellular carcinoma (NBNC-HCC) has become larger and larger as decreasing viral-HCC in Japan, and we often encounter HCC patients without hepatic fibrosis (F0-HCC). We aimed to elucidate the clinical characteristics and prognosis of F0-HCC patients.
Methods: From 2000 to 2023, 505 patients (median 70 years, 397 males), who underwent resection as an initial treatment, were enrolled. According to positivity of hepatic fibrosis, they were divided into 2 groups (F0 n=59, and Fibrosis groups n= 446), and the period of coverage was divided into six-year intervals. Clinical features were compared, retrospectively (IRB26-11).
Results: The ratios of NBNC-HCC (5.1/3.9/8.2/18.6%) and those with F0-HCC (1.3/7.0/13.3/20.0%) of each period became larger (each $p<0.01$). The F0 group was older (75 vs. 69 years) and showed a higher NBNC-HCC ratio (67.8 vs. 21.3%) (each $p<0.01$). Although there were no differences in Child-Pugh and ALBI between both groups, the F0 group showed better platelet counts, prothrombin time, albumin, and total-bilirubin, AFP levels (4.8 vs. 14.9 ng/mL), and larger tumor size (6.2 vs. 4.2cm), and multi-tumor (10.2 vs. 26.2%) (each $p<0.05$). F0 group had a better prognosis (median overall survival: not arrival vs. 90.6 months) and recurrence free survival (median 67.2 vs. 35.1 months) using inverse probability weighting methods (each $p<0.01$).
Conclusion: The ratio of F0-HCC patients, of whom elderly and NBNC were majority, has become larger. Even patients with massive hepatocellular carcinoma have a good prognosis if radical surgery can be performed and there is no hepatic fibrosis.

P-50
10046

Second-Line Treatment Strategy in Unresectable Hepatocellular Carcinoma after First-Line Atezolizumab Plus Bevacizumab

Kunihide Mohri, Takanori Mukozu, Teppei Matsui, Hideki Nagumo, Naoyuki Yoshimine, Noritaka Wakui, Hidenari Nagai
Department of Gastroenterology and Hepatology, Toho University Medical Center Omori Hospital, Tokyo, Japan

Background: Atezolizumab plus bevacizumab (AteBev) are an integral part of first-line therapy for unresectable hepatocellular carcinoma (uHCC), whereas no second-line regimen has been developed for these patients. In this study, we evaluated the efficacy of lenvatinib (LEN) as second-line therapy for uHCC following AteBev treatment.
Methods: Sixty uHCC patients who were administered AteBev therapy were included in the study. Dynamic computed tomography was conducted after 6, 9, and 12 weeks, and blood tests were performed at baseline and after three weeks.
Results: After six weeks of AteBev therapy, 19 patients experienced PR, 12 had SD, and 29 exhibited PD, for ORR of 31.7%. Thirty patients underwent second-line treatment. Of the 21 patients treated with LEN, one dropped out, 9 experienced CR or PR, and 11 had SD or PD. The ORR for LEN as second-line therapy after AteBev treatment was 45.0% and DCR was 75%. The median PFS time was 3.5 months, and MST was 24.2 months. Serum levels of FGF-19 increased substantially following LEN therapy in the former, although the levels decreased significantly in the latter. Soluble FGF-R4 levels did not differ significantly between the groups when assessed before and after LEN treatment.
Conclusion: LEN was useful as second-line treatment for uHCC after AteBev therapy. Changes in serum FGF-19 levels after three weeks of AteBev therapy may serve as a biomarker for selecting LEN as second-line therapy.

P-51
10074

Influence of Gender Differences and Aging on the Clinical Background of Patients with Hepatocellular Carcinoma

Atsushi Hiraoka[1], Fujimasa Tada[1], Tomoyuki Ninomiya[1], Masashi Hirooka[2], Yoichi Hiasa[2]
[1]Gastroenterology Center, Ehime Prefectural Central Hospital, [2]Department of Gastroenterology and Metabology, Ehime University, Japan

Background/Aim: There have been few studies on the clinical presentation of hepatocellular carcinoma (HCC) from the viewpoint of aging and sex differences. This study aimed to clarify the influence of aging and sex differences on clinical features of HCC patients.
Materials/Methods: From 2000 to 2023, 2108 HCC patients (1518 males and 590 females) with first-episode HCC diagnosed were enrolled. They were divided into two age groups (<75 years and 75 years and older(elderly)), and the clinical features of age and sex differences were examined retrospectively by dividing the observation period into three periods.
Results: The proportions of women in periods 1 (2000-2007), 2 and 3 (2016-2023) remained unchanged at 25.5%, 30.1% and 27.6%, respectively; the proportion of elderly increased from 24.4% in period 1 to 45.5% in period 3 in patients overall. The proportion of elderly increased from 20.0% to 41.2% in men, while it increased from 37.2% to 56.7% in women (each P<0.001). Proportion of HCV/NBNC changed from 71.9%/18.0% in stage 1 to 38.0%/51.8% in stage 3 in men, and from 76.3%/15.4% to 49.2%/42.2% in women. Overall survival (OS) did not differ among elderly patients of both gender (52.6 vs. 52.9 months, P=0.568), but there was a significant difference among younger patients (<74 years) (61.7 vs. 82.4 months, P<0.01) and consequently also among patients overall (59.3 vs. 64.5 months, P=0.01).
Conclusion: The etiology changed in both gender as they aged. On the other hand, women may have a better prognosis than men when aged 74 years or younger.

P-52
10088

Real World Data of Cabozantinib in Patients with Hepatocellular Carcinoma: Focusing on Dose Setting and Modification

Hironao Okubo[1], Hitoshi Ando[2], Shunsuke Nakamura[1], Yusuke Tasaki[1], Koichi Ito[1], Yuka Fukuo[1], Kenichi Ikejima[3], Hiroyuki Isayama[3]
[1] Department of Gastroenterology, Juntendo University Nerima Hospital, Tokyo, Japan, [2]Department of Cellular and Molecular Function Analysis, Kanazawa University , [3]Department of Gastroenterology, Juntendo University School of Medicine, Japan

Aim: To investigate the outcomes of cabozantinib in patients with unresectable hepatocellular carcinoma (uHCC), focusing on dose setting and modification.
Methods: We retrospectively analyzed 34 patients who received cabozantinib for uHCC. Trough concentrations (Ctrough) of cabozantinib were also measured weekly for 6 weeks in the 18 patients.
Results: Sixteen patients received more than 40 mg (high dose group), and 18 patients received 20 mg (low-dose group). Dose escalations were performed in 27.8% of the patients in the low-dose group during the first 6 weeks. Although median duration of the first dose reduction or interruption in the low-dose group was twice that in the low-dose group (28 vs. 14 days, $p < 0.001$), there were no significant differences in the relative dose intensity (RDI) during 6 weeks, progression free survival (PFS), and overall survival ($p = 0.162$, $p = 0.950$, $p = 0.817$, respectively) between the two groups. Patients who received RDI during 6 weeks more than 33.4% showed a trend toward longer median PFS ($p = 0.054$). Each serum aldolase value during the 6 weeks was significantly correlated with the Ctrough at any point ($r = 0.500$, $p < 0.001$). In multivariate analyses, aldolase more than 8.7 U/L within 2 weeks was significantly associated with the very early dose reduction or interruption (odds ratio 20.0, $p = 0.002$).
Conclusions: An initial dose of 20 mg cabozanitinb could be a safe option. The serum aldolase value could be useful for making appropriate dose modifications of cabozantinib.

P-53
10136

Comprehensive Analysis of Reaching Radiological Cancer-free Status in Advanced-stage Hepatocellular Carcinoma

Keisuke Koroki, Sadahisa Ogasawara, Makoto Fujiya, Midori Sawada, Takahiro Tsuchiya, Ryo Izai, Takuya Yonemoto, Teppei Akatsuka, Chihiro Miwa, Masanori Inoue, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Shingo Nakamoto, Naoya Kato
Department of Gastroenterology, Graduate School of Chiba University, Japan

Background: In the realm of oncology, the pinnacle of therapeutic success is achieving a state where the patient is entirely free of cancer, i.e. 'cancer-free'. This benchmark should not only apply to early-stage malignancies but should also be the standard aim for advanced-stage diseases, including hepatocellular carcinoma (HCC). Our study sheds light on the profound implications of reaching a cancer-free status in radiological assessment of patients with advanced-stage HCC.
Methods: We established a database tracking the full clinical course of all patients with HCC (from 2003-2022). We identified the initial instances of macrovascular invasion or extrahepatic spread. We defined radiological cancer-free (RCF) as cases in which no recurrence was observed for at least 2 months following curative treatment or complete response following systemic therapies. The RCF rate was examined categorized by patient background.
Results: We identified 795 patients with advanced-stage HCC. The RCF rate was 8.7%. Patients who achieved RCF had significantly better prognoses compared to those who did not ($p < 0.001$). In the decision tree analysis, the number of tumors > 7 was the strongest factor of achieving RCF status. Analysis of stage progression patterns revealed varying background characteristics at the time of advanced-stage diagnosis, with discrepancies in cancer-free rates.
Conclusion: Despite the low rate of achieving RCF status, the prognostic impact was significant. Patients with certain tumor characteristics had a higher likelihood of achieving RCF status. The distribution of tumor conditions varies based on the pattern of progression, which affects the likelihood of achieving RCF status.

P-54
10152

Real-world Experience of Cabozantinib after Immnotherapy in Patients with Unresectable Hepatocellular Carcinoma

Kaoru Tsuchiya, Yutaka Yasui, Naoki Uchihara, Kenta Takaura, Shohei Tanaka, Chiaki Maeyashiki, Nobuharu Tamaki, Hiroyuki Nakanishi, Namiki Izumi, Masyuki Kurosaki
Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Japan

Background: Recently, a prospective phase 2 study of cabozantinib (CAB) after immune checkpoint inhibitors (ICI) in patients with unresectable HCC (u-HCC) showed that the median progression-free survival (PFS) and overall survival (OS) were 4.1 and 9.9 months. We investigated the clinical outcome of CAB after ICI in real-world practice.
Methods: Forty-three u-HCC patients who received CAB after ICI at our institution between Jan 2021 and Mar 2024 were enrolled. Tumor assessments by RECIST ver1.1 were done using dynamic CT or MRI. Adverse events (AEs) were reported according to CTCAEv5.0.
Results: The median age was 74 years, and 33 patients were Child-Pugh A. BCLC stage A/B/C were 0/ 14/ 29 patients, and 42 patients were previously treated with atezolizumab plus bevacizumab. CAB was introduced as 2nd (n= 6), 3rd (n= 18), 4th (n=10), 5th (n=4), 6th (n=4), 7th -line (n=1). The median PFS was 4.3 months (95%CI: 3.1-7.4), and the median OS was 11.7 months (95%CI: 7.7-23.1). The objective response rate (ORR) and disease control rate (DCR) were 11.4 and 80 %. The full dose induction (60mg/day) was not a significant factor associated with PFS and OS. The median relative dose intensity (RDI) of CAB for the first month (1M-RDI) was 33.3%, and there were no significant differences in PFS and OS between the patients with &gt 30% 1M-RDI (n=20) and &lt30 % 1M-RDI (n=23).
Conclusions: The clinical outcome of CAB after ICI in real-world practice was comparable with the phase 2 study. Modifying the daily dose and appropriately interrupting CAB are essential in real-world practice.

P-55
10022

Hepatocellular Carcinoma is a Prognostic Factor in Patients Treated for Esophagogastric Varices

Akira Uchiyama, Shunhei Yamashina, Masahiro Tada, Kei Iizuka, Hiroo Fukada, Kazuyoshi Kon, Kenichi Ikejima
Department of Gastroenterology, Juntendo University School of Medicine, Japan

Background: Portal hypertension (PH) and hepatocellular carcinoma (HCC) are major complications of cirrhosis and are closely related. Advanced HCC with diffuse infiltrative form or portal vein tumor thrombosis (PVTT) lead to increased PH. We investigated the prognosis of patients with HCC after endoscopic treatment of esophagogastric varices.
Methods: From 2009 to 2016, 171 cirrhotic patients with endoscopically treated esophagogastric varices were evaluated for survival rate with or without HCC or PVTT and Vp1-4 classification. Prognostic factors were analyzed using Kaplan-Meier and logistic regression analysis.
Results: The average age of the patients was 65.0±11.2 years. 59.1% of patients had HCC. The 5-year survival rate after treatment of esophageal varices was 68.3% in patients without HCC, and by each liver disease, the 5-year survival rates were 85.7% for MASLD, 75.0% for ALD, 56.3% for viral, and 60.0% for AIH/PBC. On the other hand, patients with HCC had a significantly poorer 5-year survival rate of 11.4% after varicose treatment. By comparison of Vp factors of PVTT, the 1-year survival rates were 63.6% for Vp0-2 and 50.0% for Vp3-4. Furthermore, the 5-year survival rate was 18.2% for Vp0-2 and 0% for Vp3-4. Multivariate analysis was performed as a predictor of patient prognosis, and HCC was significantly associated (odds ratio:17.655, $p<0.001$).
Conclusion: HCC was a closely related factor to prognosis after treatment of esophagogastric varices.

P-56
10037

Subharmonic-Aided Pressure Estimation (SHAPE); A New Noninvasive Technique for Diagnosing Portal Hypertension

Yoshiko Nakamura, Masashi Hirooka, Ryo Yano, Toyoki Shimamoto, Makoto Morita, Yuki Okazaki, Yusuke Imai, Takao Watanabe, Osamu Yoshida, Yoshio Tokumoto, Masanori Abe, Yoichi Hiasa
Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Ehime, Japan

Background: Portal hypertension (PH) is likely to affect the treatment progress of hepatocellular carcinoma (HCC). The standard assessment for the severity of PH is the invasive acquisition of hepatic venous pressure gradient (HVPG). Subharmonic-Aided Pressure Estimation (SHAPE) is a new noninvasive US-based method with contrast agent to evaluate the degree of PH. The purpose is to compare SHAPE gradient to HVPG to diagnose clinically significant PH (CSPH; HVPG>10mmHg).
Methods: This retrospective study enrolled patients estimated both HVPG and SHAPE gradient. SHAPE gradient was extracted from the difference between a hepatic vein and a portal vein. Correlations between data including other noninvasive tests (Fib4 index, M2BPGi, Collagen type 4, and hyaluronic acid, liver stiffness measurement (NIT)) were determined by Pearson correlation coefficient. The Area Under the Receiver operating characteristics (AUROC) analysis was performed to determine the sensitivity and specificity of SHAPE to diagnose CSPH.
Results: A total of 32 patients (median age, 73 years; 27 men; median HVPG, 8.5 mmHg; 28 patients with HCC) were included. SHAPE gradient showed a significant correlation with HVPG ($r=0.62$, $p<0.01$), which was higher than any other NITs. Patients with CSPH (n=15) had a higher SHAPE gradient compared with patients without CSPH (n=17) (-1.0 dB vs -4.9 dB, $p<0.01$), which is equivalent to a sensitivity of 73 % and a specificity of 88% with AUROC 0.835 (95% confidence interval, 0.69-0.98).
Conclusions: SHAPE could be a useful noninvasive US-based technique for assessing PH and detecting CSPH.

P-57
10058

Enhancing Bioavailability of Furosemide for the Management of Portal Hypertension Using Self Nano Emulsifying Drug Delivery System

Pankajkumar Yadav
Prayagraj Shuats, India

Background: The objective of this study was to enhance the bioavailability of furosemide (FURO), an antihypertensive loop diuretic used in the management of portal hypertension, by improving its water solubility, permeability, and absorption after oral administration. To achieve this aim, a novel drug delivery system, Self Nano Emulsifying Drug Delivery System (SNEDDS), was employed.
Methods: Various oils, surfactants, and co-surfactants were tested to determine their ability to improve the solubility of FURO. The self-emulsification region was identified using pseudoternary diagrams, and SNEDDS formulations were developed accordingly. The formulations were characterized using zeta potential determination, droplet size analysis, dilution test, viscosity determination, in vitro dissolution studies, and in vivo pharmacodynamic evaluation.
Results: Mean droplet size of the optimized formulation was found to be 26.8 nm. In vitro performance of the optimized preparation was satisfactory as observed by various analyses such as dilution test, emulsification time, and precipitation assessment. In vitro dissolution studies exhibited that the optimized SNEDDS formulation F3 exhibited a 1.7 fold increase in dissolution efficiency as compared to plain FURO and marketed formulations. In vivo studies showed enhanced bioavailability of F3 in terms of diuretic efficacy.
Conclusion: The study confirms the potential use of SNEDDS formulation as an alternative to traditional oral formulations of FURO to enhance its bioavailability in the management of portal hypertension.

P-58
10073

Significance of Neutrophil-to-lymphocyte Ratio in Bleeding after Endoscopic Treatment of Cirrhotic Patients with Esophageal Varices

Kazuto Takahashi, Takuto Nosaka, Yosuke Murata, Ryotaro Ssugata, Tomoko Tanaka, Yu Akazawa, Tatsushi Naito, Masahiro Ohtani, Yasunari Nakamoto
Second Department of Internal Medicine, University of Fukui, Fukui, Japan

Background: It is now becoming clear that Neutrophil-to-lymphocyte ratio (NLR) is a prognostic factor in patients with liver cirrhosis. Furthermore, it is significant to predict bleeding after endoscopic procedures because it can be fatal. The aim of this study was to clarify the relationship between NLR and bleeding after endoscopic treatment for esophageal varices in cirrhotic patients.
Methods: The study included 141 patients who underwent initial endoscopic treatment for esophageal varices at our hospital from April 2006 to March 2022 and were able to be followed up for more than 1 year. Endoscopic treatment included endoscopic injection sclerotherapy in 100 patients and endoscopic variceal ligation alone in 41 patients. The relationship between clinical background, including NLR, and post-treatment bleeding in patients with esophageal varices was investigated using the Kaplan-Meier method.
Results: In this cohort, median age at initial endoscopic treatment was 67.0 years, and there were 41/66/34 patients with Child-Pugh grade A/B/C. During the observation period, the cumulative non-bleeding rate after endoscopic treatment was 81.3% at 1 year and 72.9% at 3 years. The cumulative non-bleeding rate after esophageal varices treatment was significantly lower in patients with NLR ≥4.0 and serum albumin level <2.8 g/dL ($p<0.05$), and both were independent factors in the cox regression analysis. Furthermore, cumulative survival was significantly lower in patients with NLR ≥4.0, as well as post-treatment bleeding ($p<0.05$).
Conclusion: In cirrhotic patients with esophageal varices, high NLR levels may predict bleeding and poor prognosis after endoscopic treatment, by reflecting the poor general conditions.

P-59
10083

Regional Difference for Morbidity of Liver Cancer and Spread of Ultrasound Elastography in Japan: A Real-world Evidence Using National Database of Health Insurance Claims

Masahito Nakano[1], Machiko Kawaguchi[1], Dan Nakano[1], Tomoya Sano[1], Keisuke Amano[1], Toru Nakamura[1], Hirokazu Takahashi[2], Kunio Tarasawa[3], Kenji Fujimori[3], Takumi Kawaguchi[1]
[1]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, [2]Liver Center, Saga University Hospital, [3]Department of Health Administration and Policy, Tohoku University School of Medicine, Japan

Background: The etiology of liver cancer is changing from hepatitis virus to metabolic dysfunction-associated steatotic liver disease and ultrasound elastography is useful to capture patients at high risk. We aimed to investigate the regional difference in the prevalence of liver cancer and the use of ultrasound elastography in Japan using National Database of Health Insurance Claims (NDB).
Methods: We used NDB open data in 2020. The total number of claims was approximately 944 million. The Standardized Claims Data Ratio (SCR) was employed to evaluate regional differences. We investigated the medical receipt information of liver cancer and elastography by 47 prefectures. The 47 prefectures were categorized into 8 administrative regions.
Results: The highest SCR of liver cancer was observed in Kyushu (median 134, IQR [109–139]), followed by Chugoku (113, [110–132]), Kinki (109, [89–126]), and Shikoku regions (107, [100–121]), especially in western Japan. Higher SCR was also observed in the treatment of liver cancer such as hepatic resection and radiofrequency ablation in western Japan. However, the SCR of transient elastography was low in many prefectures throughout Japan, even in western Japan. Similarly, the SCR of shear wave elastography was low in many prefectures throughout Japan, even in western Japan.
Conclusion: The morbidity of liver cancer was high in western Japan. On the other hand, ultrasound elastography was not widely used throughout Japan. There is an urgent need to promote awareness of ultrasound elastography to screen patients at high risk for liver cancer, particularly in western Japan.

Poster Session

P-60
10120

Efficacy and Safety of Avatrombopag

Rie Goka, Naoki Morimoto, Shunji Watanabe, Mamiko Tsukui, Yoshinari Takaoka, Hiroaki Nomoto, Hiroshi Maeda, Wataru Ueno, Yosuke Otsuka, Kouichi Miura
Division of Gastroenterology, Department of Medicine, Jichi Medical University, Japan

Background: Patients with advanced chronic liver disease (CLD) such as cirrhosis often have thrombocytopenia associated with increased splenic function. On the other hand, patients with CLD, including hepatocellular carcinoma may require invasive procedures with the risk of bleeding for examinations and treatments. In these cases, platelet transfusion is sometimes required to reduce the risk of bleeding complications. In 2015, the administration of lusutrombopag became available, and we have experienced cases in which platelet transfusion could be avoided. Avatrombopag, which was newly approved in 2023, is no need to check platelet counts 5 days after administration, so it is considered more useful in clinical setting. In this study, we examined the efficacy and safety of avatrombopag.
Methods: Eight patients with CLD who received avatrombopag between June 2023 and June 2024 were retrospectively evaluated for serological parameters, Spleen Index, and platelet increase.
Results: The median Spleen Index was 92.0 cm^2 (22.1-112.5) and the median platelet count before administration of avatrombopag was $4.9\times10^3/\mu L$ (3.6-5.0). All patients showed an increase in platelets, and platelet counts increased to over $5.0\times10^3/\mu L$, therefore, platelet transfusion avoidance rate was 100%, and no hemorrhagic event occurred.
Conclusions: Avatrombopag was useful in safely and effectively increasing platelet counts in patients with CLD and thrombocytopenia who were scheduled to undergo invasive procedures. In addition, there is no need to check platelet counts after the administration of avatrombopag, so it is considered to be beneficial in clinical practice use.

P-61
10143

The Diagnostic Ability of the Prediction for Hepatocarcinogenesis Using Non-invasive Scoring Systems Including VCTE and CAP in Patients with MASLD/MASH

Takashi Nishimura[1,2], Nobuhi Aizawa[1], Tomoyuki Takashima[1], Yukihisa Yuri[1], Naoto Ikeda[1], Shinya Fukunishi[1], Hideyuki Shiomi[1], Hiroko Iijima[1], Hirayuki Enomoto[1]
[1]Department of Gastroenterology, Hyogo Medical University, [2]Ultrasound Imagiing center, Hyogo Medical University Hospital, Japan

Background And Aims: Various non-invasive scoring systems for the degree of liver fibrosis in NASLD/NASH patients have been developed. The aim of this study was to clarify the diagnostic ability for the prediction of hepatocarcinogenesis using non-invasive scoring systems in MASLD/MASH patient.
Methods: The 741 MASLD/MASH consecutive patients from October 2014 to March 2023 who underwent vibration-controlled transient elastography (VCTE) and controlled attenuation parameter (CAP) were included in this retrospective cohort study. Non-invasive scoring system were FAST score, Agile 3+ and Agile 4. The prediction of hepatocarcinogenesis by VCTE also investigated.
Results: 10 out of 741 MASLD/MASH patients (1.3%) developed hepatocellular carcinoma(HCC). The cumulative hepatocarcinogenesis rate was 0.4, 1.1, 1.4% in 1, 3, 5 years, respectively. Hazard ration(HR) for hepatocarcinogenesis using FAST score with cutoff value 0.67 was 7.33(95%CI; 2.04-26.3)(p=0.002) and C-index was 0.601. Hazard ration(HR) for hepatocarcinogenesis using Agile 3+ with cutoff value 0.679 was 8.10(95%CI; 1.71-38.3)(p=0.008) and C-index was 0.68. HR for hepatocarcinogenesis using Agile 4 with cutoff value 0.251 and 0.565 were 7.25(95%CI; 1.537-34.19)(p=0.012) and 8.08(95%CI; 2.26-28.9) (p=0..001), respectively. C-index with cutoff value 0.251 and 0.565 using Agile 4 were 0.677 and 0.643, respectively. HR for hepatocarcinogenesis using VCTE with cutoff value 7.6(kPa) and 9.6(kPa) were 5.24(95%CI; 1.475-18.62)(p=0.010) and 8.74(95%CI; 2.458-31.04) (p<0..001), respectively. C-index with cutoff value 7.6 and 9.6 using VCTE were 0.616 and 0.653, respectively.
Conclusion: Each non-invasive scoring system was useful for the prediction of hepatocarcinogenesis in MASLD/MASH patients.

P-62
10011

Effects of SGLT2 Inhibitors on the Onset of Extrahepatic Cancer in Type 2 Diabetic Patients with MASLD: A Nationwide Database Study in Japan

Takumi Kawaguchi[1], Yoshiyuki Fujishima[2], Fusayo Io[2], Yuri Sato[2], Saeko Uchida[2], Yukiko Kitajima[2]
[1]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Japan, [2]Taisho Pharmaceutical Co., Ltd., Tokyo, Japan

Backgrounds: Sodium-glucose transporter 2 inhibitors (SGLT2i) have been reported to improve hepatic steatosis in patients with type 2 diabetes mellitus (T2DM) and metabolic dysfunction-associated steatotic liver disease (MASLD). We aimed to investigate the impact of SGLT2i on the incidence of extrahepatic cancer compared with dipeptidyl-peptidase 4 inhibitors (DPP4i) using a nationwide medical claims database in Japan.
Methods: We conducted a retrospective cohort study using a large-scale Japanese medical claims database from 2014 to 2022 (Medical Data Vision). From T2DM patients prescribed SGLT2i or DPP4i (n=1,628,656), eligible patients with MASLD were classified into SGLT2i (n=4,204) and DPP4i (n=4,204) groups after propensity score matching. Effects of SGLT2i on the following outcomes were compared to DPP4i: Outcome 1) changes in HbA1c and ALT levels after 6 months and 2) the incidence of extrahepatic cancer over 12 months.
Results: 1) After 6 months, DPP4i significantly decreased HbA1c levels than SGLT2i (P<0.01). In contrast, SGLT2i significantly decreased ALT levels than DPP4i (P<0.01). 2) SGLT2i significantly suppressed the incidence of extrahepatic cancer (HR 0.50, 95%CI 0.30-0.84) compared to DPP4i. Particularly, this beneficial effect of SGLT2i was further evident in patients with age ≥65 years (HR 0.37, 95%CI 0.19-0.70), with ALT >30 U/L (HR 0.52, 95%CI 0.27-0.99), and with HbA1c <7.0% (HR 0.29, 95%CI 0.10-0.80).
Conclusions: SGLT2i was more beneficial than DPP4i in improving hepatic inflammation. Moreover, SGLT2i suppressed the incidence of extrahepatic cancer compared to DPP4i. Thus, SGLT2i may be beneficial in suppressing life-threatening events in patients with T2DM and MASLD.

P-63
10090

Effect of MAFLD on Hepatocarcinogenesis in HBeAg-negative Patients with Undetectable HBV-DNA under NA Therapy: A Multicenter Study

Keisuke Amano[1,2], Tomoya Sano[1,2], Tatsuya Ide[1,2,3], Dan Nakano[1], Tsubasa Tsutsumi[1], Teruko Arinaga-Hino[1], Machiko Kawaguchi[1], Shingo Hirai[4], Ichiro Miyajima[5], Takuji Torimura[6], Takumi Kawaguchi[1]
[1]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Japan., [2]Consulting and Support Center for Liver Diseases Fukuoka, Kurume University Hospital, Kurume, Japan., [3]Kurume University Medical Center, Kurume, Japan., [4]Department of Gastroenterology, Public Yame General Hospital, Yame, Japan., [5]Department of Gastroenterology, Kumamoto Central Hospital, Kikuchi, Japan., [6]Department of Gastroenterology, Omuta City Hospital, Omuta, Japan

Background and Aims: Progression of liver fibrosis and males are risk factors for hepatocarcinogenesis under nucleos(t)ide analogs (NAs) therapy. Metabolic dysfunction-associated fatty liver disease (MAFLD) is also a risk factor for hepatocarcinogenesis. This study aims to investigate factors involved in hepatocarcinogenesis under NAs therapy, including MAFLD.
Subjects and Methods: This study is a retrospective study (observation period: median 9.4 years [2.1-19.6 years]). The subjects were 164 patients taking NAs for more than 2 years and were HBeAg-negative and undetectable HBV-DNA. They had no history of hepatocellular carcinoma (HCC). We investigated the profile of the onset of HCC under NAs therapy using decision tree analysis.
Results: HCC developed in 20.7% (34/164) during the observation period. The prevalence of MAFLD in the HCC group was significantly higher than that in the non-HCC group (64.7% vs. 43.9%, P=0.03). Particularly, in the low-medium risk group classified by PAGE-B, MAFLD increases the risk of HCC development. In multivariate analysis, FIB-4 index≥2.67, male, and MAFLD (OR 2.4, 95%CI 1.0-6.0, P=0.04) were independent factors associated with the onset of HCC. In a decision tree analysis, MAFLD was the second classifier for the onset of HCC next to the FIB-4 index (MAFLD 62.5%, non-MAFLD 28.5%).
Conclusions: We found that MAFLD was an independent risk factor for HCC in HBeAg-negative patients with undetectable HBV-DNA by NAs therapy. We further revealed that MAFLD was the second classifier for hepatocarcinogenesis next to the FIB-4 index. MAFLD seems to have a synergetic impact on hepatocarcinogenesis with hepatic fibrosis.

Poster Session

P-64
10116

Modified Forms of Secondary Bile Acid Levels Could be Biomarkers of Hepatocellular Carcinoma Pathogenesis in MASLD Patients

Yoshimi Yukawa-Muto[1], Hideki Fujii[1], Tomonori Kamiya[2], Norifumi Kawada[1], Naoko Ohtani[2]
[1]Department of Hepatology, Graduate School of Medicine, Osaka Metropolitan University, [2]Department of Pathophysiology, Graduate School of Medicine, Osaka Metropolitan University, Japan

Background: Gram-positive gut microbial metabolite, deoxycholic acid (DCA), reportedly promotes MASLD-associated HCC development in mice (Nature, 2013). To confirm this in human, we measured a series of serum bile acid levels in MASLD-HCC patients.
Methods: The study includes 20 healthy controls (HC) and 50 MASLD patients (35 non-HCC and 15 HCC), and the comparative analyses were conducted measuring a series of serum bile acid levels as follows: a) a comparative analysis between two subgroups among 15 HCC patients: 6 patients with ursodeoxycholic acid (UDCA) treatment and 9 patients without UDCA treatment. b) a comparative analysis across three groups of HC, MASLD-non-HCC and MASLD-HCC.
Results: a) In the UDCA-treated group, levels of UDCA and its glycine and taurine conjugates were significantly higher than in the untreated group. However, no significant differences were detected in other bile acid levels. b) In the HCC group, glycine and taurine conjugated DCA levels were higher than in the HC groups. Moreover, levels of lithocholic acid (LCA) and 3-oxo-LCA were significantly higher than in the non-HCC group.
Discussion: In literature, 3-oxo-LCA inhibits Th17 cell differentiation (Nature, 2022), and Th17 cells promote cytotoxic T cell activation in tumor immunity (Immunity, 2009). The increased levels of 3-oxo-LCA in MASLD-HCC patients might suppress Th17 cell differentiation, thereby inhibiting antitumor immunity to promote HCC.
Conclusion: LCA and 3-oxo-LCA levels as well as glycine and taurine conjugated DCA levels were elevated in the HCC group. Further investigation is needed to elucidate the mechanisms involving 3-oxo-LCA in HCC carcinogenesis.

P-65
10122

Efficacy of Measuring Natural Killer-activating Receptor Ligands to Predict the Pathogenesis of Metabolic Dysfunction-associated Steatotic Liver Disease

Jun Arai[1], Akinori Okumura[1], Satoshi Kimoto[1], Kazumasa Sakamoto[1], Tomoya Kitada[1], Rena Kitano[1], Tadahisa Inoue[1], Sayaka Nishimura[1], Noriko Inden[1], Yukiko Muraki[1], Naoya Kato[2], Kiyoaki Ito[1]
[1]Department of Gastroenterology, Aichi Medical University, Nagakute, Aichi, Japan, [2]Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

Background: The number of patients with MASLD is increasing. The degree of intrahepatic NK cell infiltration has been reported to correlate with MASLD progression. However, reports on MASLD are limited. We aimed to investigate the involvement of NK cell-activating receptor ligands in MASLD pathogenesis.
Methods: This study cohort comprised 72 patients with biopsy-proven MASLD treated between 2012 and 2018 at our institute. The concentrations of major histocompatibility complex class I polypeptide-related sequences A and B (MICA and MICB, respectively) and B7H6 in patient sera were measured using ELISA kits. The clinical characteristics related to higher concentrations of each NK cell-activating receptor ligand were also investigated.
Results: The MASH (n=47) group had a higher level of the ligands than the MAFL (n=25) group. Furthermore, the MASH group had a significantly higher level of the M2BPGi than the MAFL group ($P<0.01$). Logistic regression analysis after adjusting for sex, age, and body mass index revealed that MICB ($P<0.05$) and M2BPGi ($P<0.01$) were significantly correlated with MASH. All three ligands were strongly correlated with AFP and PIVKA-2. Although MICB levels positively correlated with aspartate transaminase and alanine transaminase levels, patients with higher B7H6 levels had higher M2BPGi levels and lower number of platelets.
Conclusion: The NK-activating receptor ligands were higher in the sera of the MASH group than in the MAFL group and strongly correlated with tumor markers, indicating the potential for hepatocarcinogenesis. Although MICB was correlated with the severity of intrahepatic inflammation, B7H6 was correlated with the degree of intrahepatic fibrosis.

P-66
10026

Can the Blood Coagulation Factor Von Willebrand Factor be a Predictor of Response to Atezolizumab plus Bevacizumab Combination Therapy for Advanced Hepatocellular Carcinoma?

Naoki Nishimura[1], Tadashi Namisaki[1], Hiroaki Takaya[2], Kosuke Kaji[1], Hitoshi Yoshiji[1]
[1]The department of Gastroenterology, Nara medical university, Kashihara Nara Japan, [2]Nara Prefectural Seiwa Medical Center, Japan

Purpose: We have previously reported that von Willebrand factor antigen (VWF), a blood coagulation factor, is a potential predictor of response to molecularly targeted drugs and hepatic infusion chemotherapy in patients with advanced hepatocellular carcinoma (HCC). In this study, we investigated the usefulness of VWF as a predictor of response to atezolizumab plus bevacizumab (AB) therapy for HCC.
Methods: The subjects were 58 patients with advanced HCC treated with AB. RECISTv1.1 and mRECIST were used to determine efficacy. All analyses were based on laboratory values at the start of AB therapy.
Results: Median age: 74 years, HBV/HCV/alcohol/MASLD/PBC/other: 11/13/13/12/1/8, median maximum tumor diameter: 3.7 cm, median number of tumors: 4. VWF was positively correlated with Child-Pugh score, ALBI score, PIVKA2, and number of tumors, and negatively correlated with Alb. VWF, ALBI score, and Child-Pugh score were significantly lower in the response group [CR/PR] than in the non-response group [SD/PD] in the RECIST study. In multivariate analysis, only low VWF (<135) was identified as a predictor of response. Progression-free survival (PFS) was prolonged in the low VWF group (<135) compared to the high VWF group (≤135). mRECIST showed that VWF was significantly lower in the response group than in the non-response group. Only low VWF(<135) was identified as a predictor of response in multivariate analyses. PFS in the low VWF group was prolonged compared to the high VWF group.
Conclusion: Pretreatment VWF may be a useful biomarker for predicting response to AB therapy.

P-67
10053

Interaction of PKR and 4.1R Promotes Anchorage-independent Growth of Hepatocellular Carcinoma

Yusuke Okujima[1], Takao Watanabe[1], Yoshio Tokumoto[1], Makoto Morita[1], Yuki Okazaki[1], Yusuke Imai[1], Mitsuhito Koizumi[1], Masanori Abe[1], Takeshi Imamura[2], Yoichi Hiasa[1]
[1] Department of Gastroenterology and Metabology, Graduate School of Medicine, Ehime University, [2] Department of Molecular Medicine for Pathogenesis, Graduate School of Medicine, Ehime University, Japan

Backgrounds: We have previously shown that Protein kinase R (PKR) is highly expressed in hepatocellular carcinoma, enhances cancer cell proliferation. However, the functional target molecule and the molecular mechanism have not been clarified. In this study, we aimed to identify molecules that bind directly to PKR and to analyze the role of the functional role of identified molecules on HCC.
Methods: To determine the binding molecules of PKR, mass spectrometry analysis was performed with immunoprecipitated samples. The relationship between PKR and candidate proteins were validated by co-immunoprecipitation and western blot. The function of PKR and identified binding protein were assessed by an MTT assay or a colony formation assay.
Results: Among some candidate proteins that bind to PKR with kinase activity depending manner, we focused on 4.1R. We identified that 4.1R bind to wild-type PKR, but not to kinase-deficient mutant PKR. In HCC cell lines, the expression level of 4.1R protein was shown to be regulated by PKR expression and activation. High expression of 4.1R, as well as PKR, was associated with a worse prognosis in HCC using the available online database. PKR-4.1R axis increased HCC cell growth only in an anchorage-independent manner, not in an anchorage-depending manner.
Conclusions: We found 4.1R as a new PKR binding protein and identified this PKR-4.1R interaction increases anchorage-independent growth of HCC cells.

P-68
10108

Hepatoma-derived Growth Factor as a Possible Therapeutic Target for Hepatocellular Carcinoma

Hirayuki Enomoto, Yukihisa Yuri, Tomoyuki Takashima, Nobuhiro Aizawa, Naoto Ikeda, Taro Kimura, Kohei Yoshihara, Ryota Yoshioka, Shoki Kawata, Yuta Kawase, Ryota Nakano, Hideyuki Shiomi, Takashi Nishimura, Shinya Fukunishi, Hiroko Iijima, Shinichiro Shinzaki
Department of Gastroenterology, Hyogo Medical University, Hyogo, Japan

Background: HDGF (Hepatoma-derived growth factor) is a growth factor which is involved in the progression of HCC. We have reported that HDGF is highly expressed in the HCC tissues, and the expression level of HDGF is an independent prognostic factor for the disease-free and overall survival in patients with HCC. The aim of this study is to examine whether HDGF can be a potential target molecule for the treatment of HCC.
Methods: (1) We generated the stably HDGF-overexpressed or HDGF-silenced hepatoma cell lines by the introduction of HDGF cDNA or sh-RNA, and examined the effects of the increased or reduced HDGF expression on the proliferation of hepatoma cells. (2) We investigated the effects of the exogenous and endogenous overexpression of HDGF on the proliferation and tubular formation of HUVEC (human umbilical vein endothelial cells) in vitro. (3) We examined whether the introduction of HDGF cDNA can induce the VEGF expression.
Results: (1) Introduction of HDGF cDNA promoted the proliferation of hepatoma cells, whereas reduction of HDGF by sh-RNA suppressed the growth of the hepatoma cells. (2) Administration of recombinant HDGF significantly increased the cellular number of HUVEC in vitro, and HDGF-treated HUVEC formed longer vessel-like tubes in vitro than those formed by PBS-treated control cells. (3) HDGF activated the VEGF promoter and induced VEGF expression.
Conclusions: HDGF functions as a growth stimulating factor on hepatoma cells and the other as an angiogenic factor. HDGF is therefore considered to be a possible target molecule for the treatment of HCC.

P-69
10160

Morphological Architectures of Patient-derived Hepatocellular Carcinoma Organoids with GSK3-beta Expression Dependent Variability According to Lenvatinib Resistance

Jun Yong Park, Kyungjoo Cho, Hye Jung Park
Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Background and Aims: We evaluated the potential differential sensitivity of HCC organoids(HCOs) to lenvatinib and analyzed the relationship between the resistance group of lenvatinib and intracellular signaling pathways.
Method: Patient-derived tumor tissue was digested at 37 C and mixed with Matrigel. To evaluate whether HCO exhibit different sensitivity to drugs, we tested its sensitivity and analyzed the sensitivity in HCO lines with the difference in gene expression.
Results: We successfully established HCO lines at a 76% success rate, presenting as two different morphological types: solid-type and mixed-type. Heterogeneous morphological features of HCOs exhibited differential gene expression and response to lenvatinib, showing highly expressed EGFR, GSK3-beta and FOXO3 with lower sensitivity to lenvatinib in solid type HCOs, compared to mixed type HCOs. To confirm the association of morphological classification with GSK3-beta activation and lenvatinib sensitivity, we generated a rHCO from re-biopsied tissue from a patient with HCC progression after lenvatinib treatment and compared it with the HCO established with first biopsied tissue. Specifically, the lenvatinib-resistant rHCO expressed much lower levels of the inactive form of GSK3-beta and higher levels of the active form of GSK3-beta compared with the original HCO, suggesting higher GSK3-beta activity and Ki-67 levels in resistant cells. Knockdown of GSK3-beta with selective GSK3-beta inhibitor and siRNA restores sensitivity to lenvatinib in association with GSK3-beta activity and morphological features.
Conclusion: Our work demonstrates the relationship between lenvatinib sensitivity and morphological features with GSK3-beta expression and identifies regulators of GSK3-beta activity as potential novel therapeutic agents for restoring lenvatinib sensitivity.

P-70
10166

Role of Erastin in Intestinal Injury Following Perioperative Liver Transplantation via Ferroptosis in Animals

Deepika Singh
Shalom Institute of Health and Alied Sciences, Sam Higginbittom University of Agriculture, Technology and Sciences, Prayagraj, India

Background : Perioperative liver transplantation (LT) can also result intestine damage in liver injury. Research on ferroptosis in intestinal epithelial cells reveals that the pathophysiological process of intestinal I/R damage is related to it. The point of this study was to look into how the ferroptosis activator Erastin affects LT intestinal damage in rats before surgery and to figure out how this might happen.
Methods: Collected from the portal vein (PV), inferior vena cava blood specimens were six hours and twenty-four hours respectively following I/R. We have evaluated serum interleukin 6 and serum malondialdehyde and measures of liver and intestinal damage, inflammatory and death signals
Results : We found alteration in serum transaminase (AFP, AST, ALP and AST) and the levels of intestinal MDA, and antioxidant parameters such as superoxide dismutase (SOD), glutathione (GSH), glutathione peroxidase 4 (GPX4), and tissue iron by Erastin. Western blot helped find out xCT (cysteine glutamate reverse transporter light chain protein) and GPX4 were expressed. It also mitigates the inflammatory cytokines and apoptosis (P53, Bax, B-actin and Bcl). Damaged intestinal by liver hepatic I/R in rats showed ferroptosis-mediated and supported by experimental data of ERASTIN. Further aggravated intestinal damage is corrected by Erastin which may block the cystine/glutamate antiporters /GSH/GPX4 signal axis in intestinal damage induced by I/R in rat LT liver, or iron overload after reperfusion, causing a significant accumulation of L-ROS and activating cellular ferroptosis.
Conclusions : Our studies suggest that Erastin will be beneficial drug in the management of IR following LT with underlying mechanism.

P-71
10043

A Case of Child-Pugh C with Advanced HCC Treated by a Hepatologist

Shuntaro Obi[1], Takahisa Sato[1], Naoki Takamura[1], Kentaro Takahashi[1], Ippei Yachigo[1], Shinpei Sato[1], Satoshi Murata[2]
[1]Department of Internal Medicine, Teikyo University Chiba Medical Center, Chiba, JAPAN., [2]Department of IVR Center, Teikyo university Chiba medical center, Chiba, Japan

Background: According to the Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma (HCC), Best supportive care (BSC) is recommended for Child-Pugh C patients. However, some of these patient populations may be amenable to aggressive treatment in addition to BSC.
Case: 51 yrs. old male HCV related HCC. 2017/11 liver resection, 2019/02 referred with right lobe massive+Vp4, 2019/3 PR with HAIC (Low dose FP) 1-3kur, 2020/04 1st TACE, 2020/07 HCV eradication with sofosbuvir/velpatasvir. 2020/12 2nd TACE, 2021/01 HAIC 4kur, 2022/03 3rd TACE, 2022/05 Percutaneous Transhepatic Obliteration for varices, 2022/08 PSE, 2022/09 4th TACE, 2022/12 5th TACE 2023/01 6th TACE, 2023/05 7th TACE. 2023/07 Chest wall invasion appeared and ATZ+BEV 1kur was done but stopped due to ascites. 2024/04 Prophylactic EVL was done. 2024/05 Radiotherapy was done for right chest wall invasion. 2024/06 Tremelimumab + Durvalumab was started and is being treated. He is alive 6.8 years from the initial diagnosis.
Conclusion: Some cases of poor liver function may be treatable. HCC should be treated by a Hepatologist.

P-72
10045

Atezolizumab and Bevacizumab following Stereotactic Body Radiotherapy for Two Patients with Unresectable Hepatocellular Carcinomas with Vp4/Vv3 and Vp3 Macrovascular Invasion

Satoshi Komiyama[1], Manabu Morimoto[2], Kazushi Numata[2], Shotaro Tsunoda[2], Akihiro Funaoka[2], Ritsuko Oishi[2], Akito Nozaki[2], Shin Maeda[3]
[1]Chemotherapy division, Yokohama City University Medical Center, Kanagawa, Japan,
[2]Gastroenterological Center, Yokohama City University Medical Center, Kanagawa, Japan, [3]Department of Gastroenterology, Yokohama City University Graduate School of Medicine, Kanagawa, Japan

Background: In the subgroup analysis of the IMbrave 150 trial, the prognosis of unresectable hepatocellular carcinoma (uHCC) patients with Vp4 portal vein tumor thrombosis (PVTT) remains considerably poor (median overall survival, 7.6 mo). Several studies have shown that macrovascular invasion (MVI), including Vp3, Vp4, and Vv3 (inferior vena cava tumor thrombosis), is associated with a poor prognosis in uHCC patients. Meanwhile, good local control of stereotactic body radiotherapy (SBRT) has been reported in MVI.
Case summary: A 70's female (case 1) and a 70's male (case 2) with liver-confined uHCC with Vv3 and Vp4 (case 1) and Vp3 (case 2) presented to us, with Child-Pugh A liver function. The maximum tumor diameter was 94 mm (case 1) and 52 mm (case 2). We started both patients on atezolizumab plus bevacizumab following SBRT for MVI. According to the Response Evaluation Criteria in Solid Tumors, the therapeutic effects in intrahepatic lesions were rated as partial response (time to response, 23 wk in case 1 and 13 wk in case 2), and durable response was achieved for 19 mo (case 1) and 6 mo (case 2) without adverse events leading to treatment discontinuation. Overall survival in both cases is 19 months (case 1) and 11 months (case 2), which is better than the median overall survival in the IMbrave 150 subgroup analysis of uHCC patients with Vp4.
Conclusion: atezolizumab plus bevacizumab following SBRT for MVI could be effective and safe in uHCC patients with MVI and Child-Pugh A liver function.

P-73
10060

A Case Study of Advanced Hepatocellular Carcinoma Treated with Radiotherapy and Chemotherapy

Hideo Yoshida, Koji Uchino, Hiroyoshi Taniguchi
The Department of Gastroenterology and Hepatology, Japanese Red Cross Medical Center, Tokyo, Japan

Background and Purpose: The combination of chemotherapy and locolesional therapy is expected to be effective. The purpose of this study was to examine the clinical characteristics of cases in which stereotactic radiotherapy was used as local therapy in combination with chemotherapy.
Patients and Method: The clinical course of patients with advanced hepatocellular carcinoma who underwent both stereotactic radiotherapy and chemotherapy during the course of their treatment was investigated. Radiotherapy was performed with stereotactic radiotherapy (CyberKnife) with gold marker implantation in cases where it was necessary. The safety and efficacy of combined treatment with radiotherapy and chemotherapy were examined.
Results: Eight patients were treated with radiation and chemotherapy during the above period. Five patients received lenvatinib and three received atezolizumab plus bevacizumab in the first line. The observation period was MEDIAN 27.5 months (RANGE 17.0-73.5 months). There were no specific adverse effects that could be attributed to the combination of radiation and chemotherapy within the scope of the study.
Discussion: In the present study, no specific safety or efficacy problems were found with the combination of radiation therapy and chemotherapy. Future studies are needed to examine the safety and efficacy of radiation therapy after the start of chemotherapy.

P-74
10063

A Case of Hepatocellular Carcinoma with Vp4 Treated with Durvalumab plus Tremelimumab after Lenvatinib plus Hepatic Artery Infusion Chemotherapy

Mariko Nishioka[1], Naohiro Okano[1], Yuji Saito[1], Masato Hayashi[1], Taro Sato[1], Tomonori Mizutani[1], Naohiro Uchida[2], Masahide Tokuhira[2], Ryutaro Sumi[2], Moegi Mochizuki[2], Takahiro Yamada[2], Ryosuke Kaji[2], Satowa Seki[2], Akiko Ohno[2], Naohiro Kawamura[2], Hideaki Mori[3], Fumio Nagashima[1], Tadakazu Hisamatsu[2], Shuichi Hironaka[1]
[1] Department of Medical Oncology, Kyorin University Faculty of Medicine, Tokyo, Japan, [2]Department of Gastroenterology and Hepatology, Kyorin University School of Medicine, Tokyo, Japan, [3]Department of Medical Education, Kyorin University School of Medicine Tokyo, Japan

Background: Durvalumab plus tremelimumab (DT) is a standard first-line treatment for patients with advanced hepatocellular carcinoma (HCC). Data on the efficacy and safety of DT as a second-line treatment are limited, with most previous chemotherapy regimens being atezolizumab plus bevacizumab or tyrosine kinase inhibitor monotherapy. Lesser data are available for following treatment with lenvatinib plus hepatic artery infusion chemotherapy (HAIC).
Case presentation: A 56-year-old man with a performance status of 1 was diagnosed with multiple HCC and lymph node metastases. The background liver disease etiology was alcohol consumption. He had massive ascites due to Vp4, red sign-positive esophageal varices, and a Child-Pugh score of 8. He was treated with lenvatinib plus HAIC using cisplatin without treatment of esophageal varices considering liver dysfunction, and developed progressive disease after 16 months. As he had a Child-Pugh score of 6, DT was selected as the second-line treatment. A partial response with 39.8% tumor shrinkage was achieved, and alpha-fetoprotein levels normalized to 33.3 ng/mL in 2.5 months after initiating DT. After four months, the esophageal varices began to bleed, which was treated with endoscopic variceal ligation. DT was resumed without delay in the next cycle. He has continued to undergo treatment for 10 months after initiation. Treatment-related toxicities were diarrhea (grade 1) and increased aspartate aminotransferase and alanine transaminase levels (grade 2). No immune-related adverse events occurred.
Conclusion: We report a case of HCC with Vp4 for which DT showed a good response with acceptable toxicities as a second-line treatment after lenvatinib plus HAIC.

P-75
10102

Curative Treatment of Two Hepatocellular Carcinoma Cases with Radiofrequency Ablation Following Atezolizumab Plus Bevacizumab

Kosuke Matsumoto, Yoshinari Asaoka, Akihito Takeuchi, Ryo Miura, Toshihiko Arizumi, Hiroo Imazu, Atsushi Tanaka
Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan

Background: Atesolizumab plus bevacizumab (ATZ+BEV) is a systemic therapy for unresectable hepatocellular carcinoma (HCC), and appropriate combination with local therapies such as radiofrequency ablation (RFA) and transarterial chemoembolization (TACE) is also expected to improve therapeutic efficacy. Here, we report two cases in which RFA was performed after disease control with ATZ+BEV and good outcomes were obtained.
Case 1: A male in his 50s. He had an initial occurrence of HCC due to hepatitis B nine years ago and underwent RFA. Two years ago, metastasis in the right hepatic hilum and metastasis in the left lung were detected. ATZ+BEV was introduced. During administration, both lesions shrank and achieved complete response. However, 1.5 years later, a CT scan revealed a single recurrent lesion in S4, and RFA was performed.
Case 2: A male in his 70s with alcoholic cirrhosis presented with a single 6.3 cm lesion in S1/6 with Child-Pugh class B. Efforts were made to improve liver function through abstinence from alcohol, improving to Child-Pugh class A. Given the hypovascular nature of the lesion, TACE was deemed ineffective, and ATZ+BEV was initiated. After four courses, the lesion reduced to 4.4 cm. However, ascites appeared, making the continuation of ATZ+BEV difficult. RFA was added as local therapy.
Discussion: Adding RFA at an appropriate timing allowed for tumor control.
Conclusion: Multidisciplinary treatment combining ATZ+BEV and RFA was considered an effective therapeutic approach for unresectable HCC.

P-76
10145

A Case of Vp4 Hepatocellular Carcinoma Successfully Treated with Hepatic Arterial Infusion Chemotherapy Combined with Radiotherapy (HAIC-RT) and Subsequent Molecular Targeted Therapy

Hirotoshi Ebinuma[1], Kazuaki Inoue[1], Masaaki Akahane[2]
[1]Department of Gastroenterology & Hepatolgy, International University of Health and Welfare, [2]Department of Radiology, International University of Health and Welfare, Japan

A 70-year-old man had been attending our department for hypertension, hyperlipidemia, hyperuricemia, alcoholic liver disease, and atrial fibrillation at the Cardiovascular Center. He was referred to our department about 6 years ago because of multiple hyperechoic lesions in his liver by an abdominal ultrasound, which were performed due to worsening liver dysfunction. He had been drinking beer 500 ml/day almost every day. Although his liver function was preserved (ALBI grade 2a), abdominal CT and EOB-MRI showed portal vein invasion from the main tumor in the S8 right lobe of the liver, and almost the entire portal vein branch in the liver was replaced by the tumor (Vp4). Therefore, a hepatic arterial reservoir catheter was inserted, and a total of low-dose FP chemotherapy were administered with radiotherapy (50 Gy/25 Fr.) to the portal vein tumor thrombus (PVTT). After that, lenvatinib was continued for the remaining tumor, and tumor markers (AFP, PIVKA-II) were normalized, and tumor shrinkage was observed on imaging. The patient has continued to receive lenvatinib with TACE for tumor growth, and he has been controlling his hepatocellular carcinoma for about 6 years.HAIC-RT is extremely useful for advanced liver cancer including PVTT, but the technique is difficult and there is often hesitation about when to administer it. However, since it is often successful in patients with advanced PVTT (Vp3/Vp4), we report here the results of our previous experience of HAIC-RT.

P-77
10158

A Case of a Hepatocellular Carcinoma Associated with Autoimmune Hepatitis with Atezolizumab and Bevacizumab Therapy

Kazuo Tsubura, Haruka Yamazaki, Takafumi Sakuma, Takatoshi Yamamoto, Takao Nishikawa, Shinji Morii, Shinichiro Okabe, Osamu Yokosuka
Matsudo City General Hospital,Chiba, Japan

Background: Hepatocellular carcinoma (HCC) associated with autoimmune hepatitis (AIH) is rare. Recently, immune checkpoint agents have been evaluated for their efficacy and have become the first-line treatment for HCC, but the influences of immune checkpoint agents on autoimmune diseases are still unclear. In this report, we describe a case of HCC associated with AIH, in which atezolizumab plus bevacizumab therapy was effective.
Case report: The patient is an 83-year-old woman who was diagnosed with AIH 20 years ago and had been receiving treatment. Recently, her condition had settled down and she was under observation. During the follow-up, multiple intrahepatic tumors were observed, and drug therapy was selected based on her age. Based on the patient's history, treatment was first started with lenvatinib. After 3 months of treatment, the patient was determined to have difficulty continuing the treatment due to severe fatigue, and lenvatinib was discontinued. After that. atezolizumab plus bevacizumab treatment was started, although the risk of HCC was considered. Six months after the start of treatment, imaging evaluation showed that the HCC had shrunk and there was an overall effect of PR. Bevacizumab was discontinued due to the appearance of generalized edema, but atezolizumab could be continued without any problems.

P-78
10014

Comparing Clinical Outcomes between PD-L1 and PD-1 Inhibitors Plus Anti-VEGF Antibody Combined with Hepatic Arterial Interventional Therapies in Unresectable HCC: A Single-center, Real-world Study

Yangxun Pan, Ze Yuan, Minshan Chen, Zhongguo Zhou
Sun Yat-sen University Cancer Center, Sun Yat-sen University, Guangzhou, China

Background: With the rise of anti-VEGF antibody plus PD-L1 regimens, particularly bevacizumab and atezolizumab, as the recommended first-line treatment for advanced hepatocellular carcinoma (HCC), there is a need to further explore PD-L1 and PD-1 inhibitors in combination therapies for unresectable HCC (uHCC). Integrating systemic therapies with locoregional approaches has become a potent strategy in managing uHCC. This study aims to compare clinical outcomes of atezolizumab (PD-L1 inhibitor) and sintilimab (PD-1 inhibitor), combined with either bevacizumab or its biosimilar and hepatic arterial interventional therapies (HAIT) in uHCC patients.
Methods: From January 2020 to September 2023, a retrospective analysis was conducted on 138 uHCC patients treated with HAIT and systemic therapies at our center. The cohort included 69 patients in the atezolizumab group (Bev/Ate) and 69 in the sintilimab group (Bio/Sin). The study evaluated efficacy and safety parameters.
Results: At the data cut-off, the median progression-free survival (mPFS) was 13.8 months for the Bev/Ate group and 10.0 months for the Bio/Sin group (P=0.188). The Bev/Ate cohort showed significantly extended intrahepatic mPFS compared to the Bio/Sin group (HR, 0.381; 95%CI, 0.176-0.824; P=0.018). Additionally, the Bev/Ate group had higher overall response rates (60.87% vs. 31.88%, P=0.001; 69.57% vs. 49.28%, P=0.024) as per RECIST v1.1 and mRECIST criteria. Treatment-related adverse events were comparable across both groups (P>0.050).
Conclusion: Combining atezolizumab or sintilimab with bevacizumab or its biosimilar alongside HAIT yielded similar overall PFS in uHCC patients. However, the atezolizumab-bevacizumab combination with HAIT showed superior intrahepatic PFS and control rates compared to sintilimab, warranting further validation.

P-79
10080

The Efficacy and Safety of Durvalumab + Tremelimumab for Unresectable Hepatocellular Carcinoma

Aiko Tanaka[1], S Uchikawa[1], T Kawaoka[1], Y Fujii[1], H Fujino[1], A Ohno[1], E Murakami[1], D Miki[1], M Tsuge[1,2], S Oka[1]
[1]Department of Gastroenterology, Hiroshima University Hospital, Hiroshima, Japan, [2]Liver Center, Hiroshima University Hospital, Hiroshima, Japan

Background: In recent years, durvalumab + tremelimumab combination therapy (Dur+Tre) was approved for unresectable hepatocellular carcinoma (uHCC).
Method: 52 cases of Child-Pugh A who recived Dur+Tre for uHCC from April 2023 to June 2024 were enrolled. The background was as follows. Male/Female: 46/6, median age 74 years, HBV/HCV/NBNC: 13/11/28, first line 23 cases, BCLC 0/A/B/C: 1/5/19/27, Child-Pugh score 5/6: 36/16, mALBI grade 1/2a/2b: 26/12/14, AFP 63.25 ng/ml and PIVKA-2 833.5 mAU/ml (median values). The administration method was the STRIDE regimen. The efficacy and safety were investigated.
Results: The evaluation after one course of administration were fllows, CR/PR/SD/PD/NE: 2/14/13/20/3 cases(mRECIST). Overall response rate (ORR) was 30.8%, and disease control rate (DCR) was 55.8%. All 2 CR cases were treated as first line systemic therapy. In first line cases, ORR was 60.9% and DCR was 69.6%. Frequently occurring adverse events were pruritus in 41 cases (79.0%), fatigue in 33 cases (63%), anorexia in 27 cases (52%). Grade 3 or higher adverse events included anorexia in 5 cases (10%), adrenal insufficiency and enteritis in 4 cases (8%), fatigue, hyperamylasemia, Hepatic dysfunction, in 2 cases (4%), hyperamylasemia in 4 cases (8%), interstitial pneumonia in 2 cases (4.8%), enterocolitis in 2 cases (4.8%) and interstitial pneumonia in 1 case (2.4%), Thrombocytopenia in 1 cases (2%).
Conclusion: Dur+Tre is effective as a first-line systemic therapy for uHCC. On the other hand, severe immune-mediated adverse events (imAE) occurred in some cases, we need to pay attention to the occurrence of imAE.

P-80
10113

Exploring the Safety and Efficacy of Durvalumab Monotherapy for Advanced Hepatocellular Carcinoma Patients Ineligible for Combined Immunotherapy

Chihiro Miwa[1], Sadahisa Ogasawara[1], Takuya Yonemoto[1], Sae Yumita[1], Tomomi Ookubo[3], Miyuki Nakagawa[2], Keisuke Koroki[1], Masanori Inoue[1], Naoya Kanogawa[1], Masato Nakamura[1], Takayuki Kondo[1], Shingo Nakamoto[1], Norio Itokawa[3], Masanori Atsukawa[3], Ei Itobayashi[2], Naoya Kato[1]
[1]Department of Gastroenterology, Graduate School of Medicine, Chiba University, [2]Department of Gastroenterology, Asahi General Hospital, [3]Department of Gastroenterology, Chiba Hokusoh Hospital, Nippon Medical School, Japan

Background: Following the HIMALAYA trial, durvalumab monotherapy became available for advanced hepatocellular carcinoma (HCC) in Japan. With combined immunotherapies as the standard of care, the position of durvalumab monotherapy remains unclear. We explored its safety and efficacy in advanced HCC patients unsuitable for combined therapy.
Methods: We retrospectively collected clinical data from 35 patients treated with durvalumab monotherapy for unresectable HCC between January and December 2023 at three medical institutions.
Results: At treatment initiation, liver function grades (mALBI) were 1/2a/2b/3 in 5/6/20/4 patients. Eight cases had vascular invasion and six had extrahepatic metastasis. Durvalumab was first-line in 21 patients and followed prior treatment in 11. The overall response rate was 2.9%, disease control rate 52.9%, and median treatment duration 4.5 months (95% CI, 2.7-7.4). Adverse events occurred in 22 patients: 9 liver dysfunction, 5 pruritus, 4 rash, and 3 diarrhea cases. Serious events, including 2 liver dysfunction and 1 diarrhea, led to treatment discontinuation. Five immune-related adverse events were observed; 2 received steroids for diarrhea and thyroxine for thyroiditis. All grade 3 or higher events occurred in patients on durvalumab for over six months. The mean ALBI scores showed no significant difference over time (p=0.239).
Conclusions: Durvalumab monotherapy demonstrated manageable safety and moderate efficacy in advanced HCC, potentially offering a treatment option for patients unsuitable for combined immunotherapy.

P-81
10123

Integrative Deep Learning Framework for Investigating the Role of Tumor-Associated Macrophages in Hepatocellular Carcinoma Metastasis Using Single-Cell Multi-Omics and Spatial Transcriptomics

Rifaldy Fajar[1], Sahnaz V. Putri[2], Prihantini Prihantini[3], Andi N. A. Ureng[4], Roland Helmizar[5]
[1]Computational Biology and Medicine Laboratory, Yogyakarta State University, Sleman, Indonesia, [2]Health Management Laboratory, International University Semen Indonesia, Indonesia, [3]Machine Learning for BioMedicine Laboratory, Bandung Institute of Technology, Indonesia, [4]Department of Pharmacy, Andini Persada College of Health Sciences, Mamuju, Indonesia, [5]Department of Internal Medicine, Baiturrahmah University, Indonesia

Background/Aim: Tumor-associated macrophages (TAMs) play a crucial role in the tumor microenvironment, contributing to metastasis and therapy resistance in hepatocellular carcinoma (HCC). This study aims to develop a deep learning framework integrating single-cell RNA sequencing, ATAC sequencing, and spatial transcriptomics to reveal TAMs' role in metastasis.
Methods: We analyzed multi-omics datasets from 1,200 HCC patients and 600 healthy controls. Single-cell RNA sequencing, single-cell ATAC sequencing, and spatial transcriptomics data were processed using Seurat, ArchR, and Space Ranger pipelines. Key features included TAM-specific gene expression, chromatin accessibility, cytokine profiles, and spatial patterns. We developed a deep learning model using Spatially Constrained Variational Autoencoders and Graph Convolutional Networks. The model was trained on 70% of the data, validated on 20%, and tested on 10%. Performance was evaluated using accuracy, precision, recall, and area under the receiver operating characteristic curve. Statistical significance was assessed with permutation tests and bootstrapping.
Results: The model achieved an area under the receiver operating characteristic curve of 0.96, identifying a TAM-specific metastasis signature of 210 differentially expressed genes and 300 differentially accessible regions (false discovery rate < 0.05). TAMs promoted metastasis through MMP9 and VEGFA upregulation, significantly enriched in metastatic HCC tissues ($p < 0.001$). Spatial analysis showed TAM localization in perivascular niches correlating with high angiogenic factors and microvessel density ($p < 0.001$).
Conclusions: This deep learning approach integrates multi-omics and spatial transcriptomics, revealing TAMs' role in HCC metastasis. Its high predictive accuracy offers potential therapeutic targets and improved treatment strategies. Further clinical validation is required.

P-82
10127

Re-positioning of Hepatic Arterial Infusion Chemotherapy in the Era of Systemic Therapy

Takahiro Tsuchiya, Sadahisa Ogasawara, Makoto Fujiya, Teppei Akatsuka, Midori Sawada, Chihiro Miwa, Takuya Yonemoto, Ryo Izai, Sae Yumita, Keisuke Koroki, Masanori Inoue, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Shingo Nakamoto, Naoya Kato
Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

Background and Aims: The role of hepatic arterial infusion chemotherapy (HAIC) is evolving with advancements in treatments for advanced hepatocellular carcinoma, including molecular-targeted agents and combination immunotherapy. To determine HAIC's future role, we analyzed cases involving HAIC during the era of systemic therapy.
Methods: We examined hepatocellular carcinoma patients treated with HAIC at our institution from June 2009 to September 2023. Patient background, safety, and effectiveness data were retrospectively collected and analyzed.
Results: HAIC was performed to 140 patients, with 67.9% having Child-Pugh B/C, 69.3% having Macro vascular invasion (MVI), and 30.7% having extrahepatic metastasis. The median survival time was 7.8 months (95% CI: 6.0-10.6), with an overall response rate (ORR) of 25.7% and a disease control rate (DCR) of 58.8%. Systemic therapy-naive patients showed an ORR of 14.5% and a DCR of 56.3%, while those with two or more prior regimens had an ORR of 38.7% and a DCR of 54.8%. Adverse events led to a 20% discontinuation rate. Median ALBI scores pre- and post-treatment were -1.67 and -1.66, respectively, indicating no significant change in hepatic function ($p = 0.245$). HAIC was introduced due to poor liver function in 16.0% and 51.7% of patients and due to MVI in 38.5% and 37.9% of patients during two different periods. The usage of HAIC for poor liver function has increased recently.
Conclusions: HAIC demonstrates tolerability in terms of liver function and high response rates, making it a viable option for patients unsuitable for systemic therapy or as a post-standard treatment intervention.

P-83
10139

Significance of Two Patterns of ICI Rechallenge with STRIDE Therapy in Advanced Hepatocellular Carcinoma

Takuya Yonemoto[1], Sadahisa Ogasawara[1], Chihiro Miwa[1], Sae Yumita[1], Tomomi Okubo[2], Miyuki Nakagawa[3], Keisuke Koroki[1], Masanori Inoue[1], Naoya Kanogawa[1], Masato Nakamura[1], Takayuki Kondo[1], Shingo Nakamoto[1], Norio Itokawa[2], Masanori Atsukawa[2], Ei Itobayashi[3], Michihisa Moriguchi[4], Yoshito Ito[4], Naoya Kato[1]
[1]Department of Gastroenterology, Graduate School of Medicine, Chiba University, [2]Division of Gastroenterology, Department of Internal Medicine, Nippon Medical School Chiba Hokusoh Hospital, [3]Department of Gastroenterology, Asahi General Hospital, [4]Department of Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine, Japan

Background: The issues in real-world practice with Durvalumab/Tremelimumab combination therapy (STRIDE) for advanced hepatocellular carcinoma include the feasibility of resuming Durvalumab (Dur) after high-incidence irAE/imAE and the safety and efficacy of STRIDE in Atezolizumab/Bevacizumab (Atez/Bev) pretreated patients. This study aims to analyze clinical data to explore these issues.
Methods: Clinical data from 68 patients with advanced hepatocellular carcinoma treated with STRIDE at four institutions in Japan from April to December 2023 were retrospectively collected and analyzed.
Results: Median age was 74 years, with 67 patients (98.5%) having PS 1 or lower and 62 patients (91.2%) having Child-Pugh A. Atez/Bev pretreated patients accounted for 33 cases (48.5%). Median PFS was 3.1 months, with an ORR of 10.3% and a DCR of 58.8%. Adverse events leading to treatment discontinuation occurred in 13 patients (19.1%). Among 34 patients with irAE/imAE, 14 resumed Dur, with 3 experiencing recurrence of the same irAE and 2 presenting different irAE/imAE. No recurrence of the same imAE/irAE was seen in Atez/Bev pretreated patients. In this group, ORR was 9.1% and DCR was 54.5%. Median PFS was 2.0 months for Atez/Bev pretreated patients versus 4.5 months for others ($P = 0.80$).
Conclusions: Resuming Durvalumab after irAE/imAE onset in STRIDE carries a risk of recurrence but may be reasonable with careful risk-benefit evaluation. STRIDE does not always cause recurrence of the same irAE/imAE as Atez/Bev treatment, and some Atez/Bev refractory cases achieved disease control with STRIDE.

P-84
10159

Real-World Outcomes of Durvalumab Plus Tremelimumab Combination Therapy (DT Therapy) in Unresectable Hepatocellular Carcinoma: Analysis by Treatment Line and Prognostic Factors

Naoki Uchihara, Yutaka Yasui, Kaoru Tsuchiya, Masayuki Kurosaki, Namiki Izumi
Musashino Red Cross Hospital, Tokyo, Japan

Background and Aims: Durvalumab plus tremelimumab (DT) therapy has been used in Japan since March 2023, but evidence for second-line or later treatments is lacking. This study aimed to evaluate real-world outcomes of DT therapy including patients who were administered as second or later-line treatment.
Method: We retrospectively analyzed patients who received DT from April 2023 to June 2024. Radiological response was evaluated using contrast-enhanced CT or MRI with RECIST v1.1 at 6-8 weeks and every 8-12 weeks thereafter.
Results: The study included 33 patients with a median age of 74 years and a median ALBI score of -2.27. Treatment lines were first (n=8), second (n=5), third (n=8), fourth or later (n=12). BCLC stages were B (n=11) and C (n=22). Median overall survival (OS) was 10.3 months for 1-3 line treatments and 3.9 months for 4th line or later treatments, with a median observation period of 4.4 months. Median progression-free survival (PFS) was 3.8 months for 1-3 line treatments and 1.7 months for 4th line or later (p=0.004). Objective response rate was 12.1% and disease control rate was 48.4%. Univariate analysis identified treatment line, Child-Pugh score, baseline CRP, and DCP ratio at 4 weeks compared to baseline (DCP ratio) as significant factors for OS. Multivariate analysis revealed CRP (HR 2.00, 95%CI 1.03-3.89, p=0.03) and DCP ratio (HR 1.01, 1.00-1.03, p=0.01) as significant factors. DCP ratio was an independent predictor for PFS (HR 1.01, 1.00-1.02, p=0.03).
Conclusion: The DCP ratio can be a useful prognostic factor for patients receiving DT therapy.

P-85
10013

Challenges and Scope in Deceased Donor Liver Transplantation in Bangladesh: The Dynamics of Ethics, Socio-culture and Religion

Md Ismail Gazi[1], Hema Binte Hamid[2]
[1]Department of Surgical Gastroenterology, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh, [2]Kamarkhanda Sub-district Health Complex, Sirajganj, Bangladesh

Background: Recently, the government planned to establish a liver transplantation (LT) program in Bangladesh. While living donors are preferred in Southeast Asia for socioreligious reasons, posthumous donations are crucial due to the limited donor pool and rising end-stage liver disease cases. This study explored the challenges and strategies for creating an effective deceased LT program through socio-cultural, ethical, and religious dimensions.
Methods: This qualitative study employed in-depth interviews with 20 general public and religious leaders, followed by a community survey of 300 respondents.
Results: Ethical concerns were prominent, with 87% of the respondents concerned about respect for the human body post-death and questioning the ethics of organ removal. Participants emphasized the need for a clear and respectful consent process that honors the posthumous donation wishes of donors (while alive) or their families. Religious views on organ donation varied, with 70% of religious leaders supporting it as a charitable act if religious guidelines are followed, while 30% had reservations due to different interpretations of religious texts. Culturally, strong familial bonds and communal decision-making emerged as double-edged swords, either facilitating (through collective support) or obstructing (through collective resistance) the consent process for organ donation. Misconceptions and the lack of awareness about organ donation, including religious prohibition, afterlife body integrity, eligibility concerns, medical mismanagement, and commercialization of organs, were also notable.
Conclusion: The study highlighted significant ethical concerns and varied socioreligious views on posthumous organ donation. Clear consent processes and awareness initiatives are essential to address misconceptions and promote deceased LT in Bangladesh.

P-86
10025

Influence of RFA on Liver Reserve Function in Child-Pugh B Patients with HCC within Milan Criteria

Ayaka Nakamura[1], Atsushi Hiraoka[1], Fujimasa Tada[1], Yuuka Kimura[1], Mai Fukumoto[1], Takuya matsuda[1], Kana Matsuoka[1], Hirofumi Izumoto[1], Kozue Kanemitsu[1], Shogo Kitahata[1], Tomoe Kawamura[1], Taira Kuroda[1], Eiji Tsubouchi[1], Hideki Miyata[1], Tomoyuki Ninomiya[1], Yoshiko Nakamura[2], Masashi Hirooka[2], Yoichi Hiasa[2]
[1]Department of Gastroenterology, Ehime Prefectural Central Hospital, [2]Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Japan

Background: The influence of radiofrequency ablation (RFA), which is recommended for hepatocellular carcinoma (HCC) within Milan Criteria (MC) in the Japanese HCC treatment guideline, on hepatic reserve has not been elucidated in HCC patients with Child-Pugh classification B (CP-B). We aimed to elucidate the influence of liver reserve function after RFA in HCC patients with CP-B.
Methods: From 2000 to 2022, 69 patients with CP-B and HCC within MC, who were treated with RFA as an initial treatment at our hospital, were enrolled (median age 68 years, male 41, Child-Pugh score 7:8:9=45:20:4, HCV:HBV:others=53:3:13). Clinical relative changes of liver disease function [Total-bilirubin (T-bil), Albumin, and albumin-bilirubin (ALBI) score] at pre-treatment (BL), 3 months after RFA, 6 months after RFA, and 12 months after RFA were evaluated retrospectively (IRB 26-11).
Results: Single tumors was 82.6% (n=57), and the median tumor diameter was 1.9 cm (IQR 1.5-2.5). Median overall survival was 49.6 months, and the 5-year survival rate was 35.4%. Although T-bil level was elevated significantly at 6 months and 1 year after RFA compared to BL [BL/3months/6 months/12 months=1.3/1.3/1.4/1.4 mg/dL, P=NA/0.892/0.026/0.045], albumin level (3.2/3.1/3.2/3.2 g/dL, P=NA/0.724/0.341/0.719) and ALBI score (-1.77/-1.79/-1.77/-1.81, P=NA/0.591/0.870/0.824) did not show deterioration from BL at 3, 6, or 12 months after RFA.
Conclusion: Because influence of RFA on liver reserve was small in patients with CP-B and HCC within MC, RFA can be safely performed in such patients.

P-87
10040

Indocyanine Green Applied in Unresectable Hepatocellular Carcinoma after Neoadjuvant Combination Therapy

Man Luo
Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background: Preoperational neoadjuvant targeted therapy comminated with immunotherapy for resectable hepatocellular carcinoma (HCC) progressively more widely used in the first line. The treated tumours necrotic and do not have a clear border with the active tumour, making radical resection difficult. The impact of surgical navigation by Indocyanine green (ICG) is scarce. In the study, we retrospectively investigated the clinical characteristics of patients who undergo surgery after neoadjuvant therapy with/without ICG fluoresce guidance.
Methods: This study included 39 patients with unresectable HCC who treated with anti-PD-1/anti-PD-L1 drugs combined with target drugs before surgery from October 2020 to October 2023. We classified the patients into two groups with/without Indocyanine green (ICG) guidance in operation, monitoring the laboratory examination and the survival outcomes to identify the necessary of ICG florescence.
Results: A total of 39 patients with unresectable undergo surgery after pre-treatment of immuno-combined-target therapy. Target therapy included Lenvatinib(51%), Erlotinib(28%), Bevacizumab(8%) and others(13%). Immune therapy included TQB2450(30%), Tirelizumab(23%) and others (%47). With/Without ICG (71.4% vs. 72.2%) all patients achieved R0 resection. Median postoperative survival (38 vs. 26 months) in patients show little difference due to the small sample size. Surgical results of the patients did not reveal ICG florescence navigation significantly prolong Progress Free Survival (PFS) compared to anatomical resection.
Conclusion: The study concludes that live tumor boundary assessment after preoperational systematic treatment remained to be explore. It may lead to a novel view that what is the best option for pretreated patients whether used ICG navigation during surgery.

Poster Session

P-88
10077

How Far Economics Analysis Does Matter: The Relation of Macroeconomic, Education, and Wealth with Liver Transplantation

Rosinta Hotmaida Pebrianti Purba[1], Helen Try Juniasti[1,2]
[1]Socioeconomics Research, The Pranala Institute, Yogyakarta, Indonesia, [2]Public Health, Cendrawasih University, Papua, Indonesia

Solid organ transplantation in 2022 reached 157,494 cases (GODT, 2023). Liver Transplantation (LT) ranked as the highest cases after kidney among 91 recorded countries. Besides the rapid increase on LT prevalence, it was performed only less than 10% of global needs. The prolonged outcomes vary accross different variable interaction. However, there is scarce literatures exploring the relationship of socioeconomic variables on LT incidenceUsing Global Observation on Donation Transplantation, World Bank, United Nations, and UNDP panel data year 2020-2022, this research analyze relation of socio-economic determinants with LT among 20 countries with the highest LT cases. Variables: health expenditure(%GDP), education, GDP per capita, human development index, female share of employment in senior-middle management, labor-force participation rate, and daily per capita protein supply. Using robust random effect, it is known that on average LT cases increases 9.1% yearly. The variables of health expenditure, education, GDP per capita, HDI, and female share of employment in senior-middle management have positive and significant impact on LT prevalence. The daily per capita protein supply and labor-force participation rate were insignificant impact on LT. The result indicates that wealth, education, and health budget can increase the LT by 2.1% among lower income countries and 4.2% on higher income countries. LT rate is relatively derived by national economic growth by 1%. Increasing LT prevalence indicates increasing global confidence in LT medical procedures. Besides macroeconomic variables, it is prominent to ensure the microeconomic by increase education attainment, literacy, and gender equality on professional labor.

P-89
10078

Epidemiology and Risk Factors Relating to Post-Liver Transplantation (LT) in Children

Lintong Hottua Simbolon[1], Rosinta Hotmaida Pebrianti Purba[1], Helen Try Juniasti[1,2]
[1]Socioeconomics Research, The Pranala Institute, Yogyakarta, Indonesia, [2]Public Health, Cendrawasih University, Papua, Indonesia

Pediatric liver transplantation has become the standard treatment for children with end-stage. It was successfully performed in various centers around the world due to improvement of surgical techniques and anti-rejection treatment and management. Using systematic review from reputable journal published between 2009-2023, this study aims to determine the risk factors related to post-LT in children. Based on the similarity of the dependent variable, food allergy should be considered after orthotopic liver transplantation in children less than 1 year of age which developed IgE-mediated food allergies after LT. Biliary complications (bile leaks and anastomotic site stricture) is higher in children than in adult recipients. Higher mortality on patients with biliary atresia after listing when it is also accured in children with Split-LT in segment IV. We also found that sleep problems (habitual snoring, excessive daytime sleepiness, daytime behavior difficulties, and RLS) are non-negligible in children after living donor liver transplantation and predicted significant variance on HRQoL. Assessment score shows that children after LT have poorer cognitive performance as well as on behavioural instrument. Hypogammaglobulinemia is not rare in the immediate post-LT period in children, and it may place patients at increased risk of infection. Age-matched donor liver in children less than 13 year are associated with less graft failure and decreased mortality. Innovative surgical techniques (split-graft LT) should be considered. A family-based approach encourage living healthy-lifestyle behaviors and clean environment. Children should get check BP regularly. Promotive and preventive should be massive.

P-90
10084

Outcome of Hepatectomy after Systemic Therapy in Hepatocellular Carcinoma: A Japanese Multi-Center Study

Norifumi Iseda[1], Shinji Itoh[1], Takeo Toshima[1], Tohru Utsunomiya[2], Keishi Sugimachi[3], Kazutoyo Morita[4], Mizuki Ninomiya[4], Noboru Harada[5], Ryosuke Minagawa[1], Tomoharu Yoshizumi[1]
[1]Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, [2]Department of Surgery, Oita Prefectural Hospital, [3]Department of Hepatobiliary-Pancreatic Surgery, NHO Kyushu Cancer Center, [4]Department of Surgery, Fukuoka City Hospital, [5]Department of Surgery, Saiseikai Fukuoka General Hospital, Japan

Background: In recent years, new systemic therapies have been developed in the field of hepatocellular carcinoma (HCC). There is little evidence concerning survival after surgery in patients with HCC who have received systemic therapies. The aim of this study was to evaluate whether post- systemic therapies hepatectomy in patients with oncologically and technically unresectable HCC improves cancer specific survival (CSS).
Methods: Data were analyzed retrospectively from 27 patients who underwent hepatectomy for HCC after systemic therapies from 6 facilities. CSS and recurrence-free survival (RFS) after hepatectomy were investigated using Kaplan-Meier curves. We examined the prognostic value of oncological criteria of resectability for HCC reported by the Japanese Expert Consensus 2023.
Results: Of the 27 cases, R0 resection was performed in 24 cases. Response Evaluation Criteria in Solid Tumors (RECIST) showed complete response (CR) in 0 patients, partial response (PR) in 16 patients, stable disease (SD) in 6 patients, and progressive disease (PD) in 2 patients. In modified RECIST, there was 1 case of CR, 20 cases of PR, 1 case of SD, and 2 cases of PD. Median CSS was could not be evaluated. Median RFS was 17.8 months. Resectable (R) and borderline resectable (BR) 1 patients had a better prognosis than BR2 patients. The group whose oncological criteria were improved by systemic therapy had a lower recurrence rate than the maintained group, but no difference was observed in CSS.
Conclusions: R and BR1 groups had a better prognosis with hepatectomy after systemic therapy compared with the BR2 group.

P-91
10128

Efficacy and Safety of Superselective Transarterial Chemoembolization Combined with Systemic Therapy for Unresectable Hepatocellular Carcinoma: A Single-Center Retrospective Cohort Study

Takuya Watanabe, Hidekatsu Kuroda, Asami Ito, Ippeki Nakaya, Hiroaki Abe, Yudai Fujiwara, Abe Tamami, Akiko Suzuki, Kei Endo, Yuuichi Yoshida, Keisuke Kakisaka, Takayoshi Oikawa, Kei Sawara, Akio Miyasaka, Takayuki Matsumoto
Division of Gastroenterology and Hepatology, Department of Internal Medicine, Iwate Medical University School of Medicine ,Tokyo, Japan

Objective: The combination of systemic therapy and transarterial chemoembolization (TACE) is a promising treatment concept for unresectable hepatocellular carcinoma (u-HCC). Superselective TACE is speculated to be an essential component of this approach, targets the subhepatic artery or most distal subhepatic septal artery; however, its efficacy and safety remains unclear. This study was designed to assess the potential of this combined treatment by focusing on the efficacy and safety of combining superselective TACE with systemic chemotherapy.
Methods: We enrolled a single-center cohort of 29 patients with u-HCC treated with lenvatinib (n =15) or atezolizumab + bevacizumab (n =14) and TACE combination therapy between 2021 and 2023. We retrospectively compared the clinical outcomes, such as tumor response, overall survival (OS), progression-free survival (PFS), and changes in ALBI score, between the superselective (SS) group and non-superselective (NSS) groups. Treatment efficacy was assessed using contrast-enhanced CT images after two courses of systemic therapy after TACE according to RECIST version 1.1 criteria.
Results: The objective response rate (ORR) and disease control rate (DCR) in the SS group (n = 17) were 64.7% and 94.1%, respectively. In contrast, the ORR and DCR in the NSS group (n = 12) were 25.0% and 58.3%, respectively with significant differences (p =0.01). The median follow-up was 23.4 months; the median OS and PFS were 46.2 and 15.9 months in the SS group and 23.4 and 4.4 months in the NSS group (p = 0.02), respectively.
Conclusions: Superselective TACE may provide clinical benefit when combined with systemic chemotherapy and TACE for patients with u-HCC.

P-92
10003

Targeting Ferroptosis with Polymerized Platinum (IV) Prodrugs Nanoparticles with Everolimus for Enhancing Therapeutic Efficacy on Cholangiocarcinoma

Yang Chen[1], Jia Huang[2], Hanchen Zhang[3], Zheng Cao[4], Haiqin Song[5], Zhiying Yang[2]
[1]Faculty of Hepato-Biliary-Pancreatic Surgery, The First Medical Center of Chinese People's Liberation Army (PLA) General Hospital, Beijing, China, [2]Department of General Surgery, China-Japan Friendship Hospital, Beijing, China, [3]University of Chinese Academy of Sciences, Beijing, China, [4]Department of Chemical and Biomolecular Engineering, University of California, Los Angeles, CA, USA, [5]Department of General Surgery, Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai, China

Background: Cholangiocarcinoma (CCA) is the second most common primary liver cancer with rising incidence globally. The majority of CCA patients are diagnosed with unresectable or metastatic disease. Traditional chemotherapy (cisplatin) and targeted drugs (everolimus) have limited efficacy and undesired toxicity in treating advanced CCA. Previous studies showed that ferroptosis is highly related to CCA. Furthermore, it was found that cisplatin and everolimus (mTORC1 inhibitor, Ev) could trigger the ferroptosis. Therefore, combining cisplatin and everolimus may be a potential approach for ferroptosis-targeted and synergistic therapy of CCA.
Methods: A glutathione (GSH) sensitive degradable amphiphilic polymer Poly-CisPt (IV) was synthesized. Then, Poly-CisPt (IV) was self-assembled with hydrophobic everolimus to form nanoparticle NP@Ev, which targeted induction of ferroptosis of CCA cells.
Results: Our study indicated that NP@Ev effectively induced ferroptosis by depleting GSH and inhibiting GPX4 and SCD1. In Vivo, NP@Ev significantly inhibited the progression of human cholangiocarcinoma in murine models with limited toxicity.
Conclusion: This work is expected to shed light on the comprehensive treatment of CCA via ferroptosis induction and facilitate the development of effective cancer nanomedicine.

P-93
10010

Examination of Interactions Affecting Epithelial-mesenchymal Transition in Intrahepatic Cholangiocarcinoma

Takahiro Haruna[1], Mitsuhiro Kudo[2], Junji Ueda[1], Kousuke Ishino[2], Daigo Yoshimori[1,2], Ryuji Ohashi[2], Hiroshi Yoshida[1]
[1]Department of Gastrointestinal Hepato-Biliary-Pancreatic Surgery, Nippon Medical School Hospital, Tokyo, Japan, [2]Department of Integrated Diagnostic Pathology, Nippon Medical School, Tokyo, Japan

Background: The interactive feedback loop among Epithelial Splicing Regulatory Protein 1 (ESRP1), Zink-finger and E-box binding 1 (ZEB1), CD44 regulate tumor progression via epithelial-mesenchymal transition (EMT); these role in intrahepatic cholangiocarcinoma (ICC) has not been investigated.
Materials and Methods: Three ICC cell lines (HuCCT-1, SSP-25, KKU-100) were used to analyze tumor behavior in Vitro. Proteomics analysis identified common proteins in the interactive feedback loop and EMT.
Results: ESRP1 expression was higher in HuCCT-1 and SSP-25 than in KKU-100. ESRP1 siRNA-treatment of HuCCT-1 and SSP-25 accelerated cell migration and invasion, ZEB1, CD44s (CD44 standard), N-cadherin and Vimentin were upregulated. Conversely, ZEB1 siRNA-treated KKU-100 upregulated ESRP1, CD44v (CD44 variants) and E-cadherin. Moreover, Proteomics analysis identified flotillin 2 as a common protein in these feedback loop and EMT.
Conclusion: These results suggest the crucial role of ESRP1 and ZEB1 and their interaction with CD44 and flotillin 2 in promoting EMT. These insights could provide novel therapeutic strategies for managing intrahepatic cholangiocarcinoma.

P-94
10031

Perioperative Outcomes of Robotic Radical Resection for Gallbladder Cancer: A Single-center Case Series

Ji-Min Dai, Xuan Zhang, Rong Liu
Faculty of Hepato-pancreato-biliary Surgery, the First Medical Center of PLA General Hospital, Beijing, China

Background: Both diagnosed and dead cases of gallbladder cancer (GBC) in Asia accounted for over 70% of the total worldwide in 2020. Radical resection is considered the most effective treatment for GBC. As robotic surgery has been applied in malignancies of liver, pancreas and biliary duct, safety and feasibility of robotic radical resection for GBC remains to be supported. We report a large case series following robotic radical resection for GBC.
Methods: Baseline characteristics and perioperative outcomes of 151 patients undergoing robotic radical resection for GBC from 2015 to 2021 were analyzed with appropriate methods.
Results: The patients were (62.8±10.4) years old, 15.9% with American Society of Anesthesiologists (ASA) score≥III, 4.7% accepting neoadjuvant therapy and 19.9% with history of minimally invasive upper abdominal surgery. The rates of conversion, transfusion and reoperation were 0.8%. Operative time was 190 (142-235) minutes and intraoperative blood loss was 50 (50-100) mL. 84.1% cases underwent hepatectomy and 4.6% underwent hepaticojejunostomy. R0 resection rates of liver and bile duct were 98.3% and 95.8%, respectively. 9 patients were admitted to ICU but no more than 5 days. The overall morbidity was 7.3% and the major morbidity (Clavien-Dindo Grade≥IIIa) was 4.0%. Five patients underwent readmission within 90 days because of unhealed wound, delayed gastric emptying, bile duct infection, bile leakage and hemorrhage of alimentary tract, respectively, while the 90-day mortality was 0%.
Conclusion: Robotic radical resection is a viable treatment for selected patients with GBC. Further studies are required to reveal long-term outcomes.

P-95
10068

High-precision Genomic Analysis Using the Molecular Barcoding Method in Liquid Biopsy of Pancreaticobiliary Cancer

Miho Sakai[1,2], Hiroshi Ohyama[1,2], Yosuke Hirotsu[2], Kenji Amemiya[2], Sumio Hirose[3], Toshio Oyama[4], Yuji Iimuro[5], Yuichiro Kojima[3], Rintaro Mikata[1], Hitoshi Mochizuki[2,3], Naoya Kato[1], Masao Omata[2,3,6]
[1]Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan, [2]Genome Analysis Center, Yamanashi Central Hospital, Yamanashi, Japan, [3]Department of Gastroenterology, Yamanashi Central Hospital, Yamanashi, Japan., [4]Department of Pathology, Yamanashi Central Hospital, Yamanashi, Japan., [5]Department of Surgery, Yamanashi Central Hospital, Yamanashi, Japan., [6]The University of Tokyo, Tokyo, Japan

Background: Obtaining sufficient tissues for biomarker discovery in pancreaticobiliary cancer is difficult and liquid biopsy may be an alternative. Although conventional next-generation sequencing methods cannot detect low-frequent mutations, the molecular barcoding (MB) method may reduce false-positive variant calls. In addition, the Ion Torrent Genexus system automates the workflow, greatly improving efficiency. This study aimed to confirm the impact of MB utilization in targeted sequencing compared to conventional panels and to evaluate the optimization and accuracy of manual and automated sequencing using MB panels.
Methods: Plasma, bile precipitate, and bile supernatant from 12 patients were collected. In the Genexus system, re-sequencing was performed in addition to MB sequencing to increase accuracy.
Results: The number of mutations per patient using the MB panel was significantly higher than that using the non-MB panel ($P = 0.002$). Tumor-derived mutations were detected more frequently using the MB panel than the non-MB panel ($P = 0.023$). The DNA yield of plasma was significantly lower than that of bile precipitate ($P = 0.02$). Although genomic analysis of plasma detected more oncogenic mutations in the manual procedure than in the Genexus system, sequencing errors were suspected. Genomic analysis of bile showed almost identical results, but KRAS mutation was detected in two patients only in the Genexus system. The turn-around time was 1 day for the Genexus system, which was 9 days shorter than the manual procedure.
Conclusion: The MB-based liquid biopsy is highly sensitive, and targeted sequencing using the Genexus system can obtain results accurately and rapidly.

P-96
10115

Effects of SGLT2 Inhibitors on Cholangiocarcinoma in Cell Lines and an Animal Model

Daisuke Minowa, Daisuke Taguchi, Yohei Shirakami, Toshihide Maeda, Hiroyasu Sakai, Masahito Shimizu
Department of Gastroenterology, Gifu University Graduate School of Medicine, Gifu, Japan

Cholangiocarcinoma (CCA), the second most common primary liver cancer, has a poor prognosis, and CCA-associated mortality has been increasing over the past decade. The sodium glucose cotransporter 2 (SGLT2) inhibitor canagliflozin (CANA) has demonstrated anti-tumor effects against several types of cancers, but its impact on CCA is unclear. This study was conducted to investigate the anti-tumor effects of CANA on CCA. CANA treatment decreased the viability of CCA cells in a concentration-dependent manner, but increased viability at low concentrations in several CCA cell lines. At high concentrations, CANA arrested the cell cycle checkpoint in the G0/G1 phase, whereas it increased the proportion of cells in the S phase at low concentrations. The findings indicated dual roles of SGLT2 inhibitor CANA in CCA. Our study also revealed CANA treatment upregulates nicotinamide phosphoribosyltransferase (NAMPT), nicotinamide adenine dinucleotide (NAD+), and sirtuin 1 in CCA cells and activates the NAD+ salvage pathway. The growth-inhibitory effect of CANA was enhanced when combined with an NAMPT inhibitor FK866. We also developed a novel rodent model of CCA induced by a carcinogen using obese mice and found that development of the malignant lesions was suppressed by administration of an SGLT2 inhibitor. These are novel and important findings in studying the effects of SGLT2 inhibitors on the malignancy.

P-97
10131

Blood CGP Pave the Way for Genomic Therapy in Biliary Tract Cancer ?

Yoshiki Ogane[1], Izumi Ohno[1], Miho Sakai[2], Kazuki Watabe[2], Yu Sekine[2], Tomoya Takahashi[2], Chihei Sugihara[2], Nana Yamada[2], Mayu Ouchi[2], Motoyasu Kan[1], Horoki Nagashima[2], Koichiro Okitsu[1], Koji Takahashi[1], Hiroshi Ohyama[2], Tsukasa Takayashiki[3], Masayuki Ostuka[3], Naoya Kato[2]
[1]Department of Medical Oncology, University of Chiba, Chiba, Japan, [2]Department of Gastroenterology, University of Chiba, Chiba, Japan, [3]Department of General Surgery, Hepato-Biliary-Pancreatic Unit, University of Chiba, Chiba, Japan

Background: Comprehensive genomic profiling (CGP) is increasingly being applied in clinical practice. While tissue-based CGP is preferred, tissue sampling can often be difficult. In such cases, cancer gene panel testing via circulating tumor DNA (ctDNA) detection in blood, known as liquid biopsy, is performed. However, blood CGP has been associated with various issues, such as low detection rates. Therefore, we investigated the utility of blood CGP in patients with biliary tract cancer.
Methods: From September 2021 to June 2024, 28 patients with biliary tract cancer who underwent blood CGP at our institution were included in this study.
Results: All cases were analyzed using FoundationOne Liquid CDx, with an average turnaround time of 12.1 days. The tumor locations included intrahepatic bile ducts (11 patients), perihilar bile ducts (7), extrahepatic bile ducts (4), and gallbladder (6). The timing of testing was at the initiation of first-line treatment (1 patient), during first-line treatment (20), at the initiation of second-line treatment (4), and after the completion of standard treatment (3). The cancer gene detection rate was 96.4%, with 14 patients having actionable mutations and 3 patients receiving targeted therapies (FGFR2: Pemigatinib, IDH1: Ivosidenib, TMB: Pembrolizumab).
Conclusion: In biliary tract cancer, blood CGP effectively detected cancer-related genes. Despite the small sample size, a comparable treatment reach rate to that of tissue-based CGP was observed. Therefore, blood CGP can be considered a useful option when tissue sampling is difficult.

P-98
10132

The Usefulness of Tissue CGP in Real-World Biliary Tract Cancer Treatment

Yu Sekine[1], Izumi Ohno[2], Yoshiki Ogane[1], Miho Sakai[1], Kazuki Watabe[1], Tomoya Takahashi[1], Nana Watabe[1], Chihei Sugihara[1], Mayu Ouchi[1], Motoyasu Kan[2], Hiroki Nagashima[1], Koichiro Okitsu[2], Koji Takahashi[2], Hiroshi Ohyama[1], Tsukasa Takayashiki[3], Masayuki Otsuka[3], Naoya Kato[1]
[1]The Department of Gastroenterology, University of Chiba, Chiba, Japan, [2]The Department of Medical Oncology, University of Chiba, Chiba, Japan, [3]The Department of General Surgery, Hepato-Biliary-Pancreatic Unit, University of Chiba, Chiba, Japan

Background: In 2019, cancer genomic profiling (CGP) tests were approved for insurance coverage in Japan, and the introduction of FGFR2 inhibitors led to increased CGP use for biliary tract cancer. We investigated the status and trends of CGP testing for biliary tract cancer at our institution.
Methods: From October 2020 to June 2024, we conducted CGP tests using Foundation One CDx on 47 biliary tract cancer patients at our institution.
Results: The average turnaround time from submission to expert panel review was 30 days. Tumor locations were intrahepatic bile ducts (24), gallbladder (11), perihilar bile ducts (6), extrahepatic bile ducts (6), duodenal papilla (2), and accessory papilla (1). Submission timing was at first-line treatment start (5), during first-line treatment (24), second-line treatment start (7), during second-line treatment (8), and post-standard treatment (3). Of 22 patients from 2020-2022, 11 (50%) were submitted during first-line treatment, compared to 18 (72%) of 25 patients from 2023-2024, indicating earlier submissions. Tissue samples were obtained by surgery (23) and biopsy (24) from liver (22), bile ducts (9), gallbladder (4), duodenum (4), and lung (3). The oldest sample had been collected 1909 days prior.
Conclusion: Our analysis of CGP testing for biliary tract cancer revealed that intrahepatic bile ducts and gallbladder were the most common tumor locations, with liver being the most frequent tissue sampling site. The trend towards earlier submission suggests that early CGP testing may expand treatment options.

P-99
10033

A Study on Hepatocellular Carcinoma and Intestinal Microflora in Patients with Chronic Hepatitis B

Yusuke Tanaka, Daiki Miki, Kenji Yamaoka, Shinsuke Uchikawa, Hatsue Fujino, Atsushi Ono, Eisuke Murakami, Tomokazu Kawaoka, Masataka Tsuge, Shiro Oka
University of Hiroshima, Hiroshima, Japan

The composition of the intestinal microbiota is highly varied among individuals. In the field of liver disease, the relationship between the intestinal microbiota and the development of chronic liver disease, fibrosis, and even carcinogenesis due to various etiologies has been reported, but a certain view has not yet been obtained. In this study, we investigated the relationship between the presence or absence of hepatocellular carcinoma and intestinal microbiota in patients with chronic hepatitis B.
Methods: The intestinal microbiota was identified in 62 patients with chronic hepatitis B using 16S rRNA analysis. The male/female ratio was 49/13, the median age was 67 years, and 46 of the 62 patients were carcinoma patients.
Results : Phylum:20, Class:41, Order:79, Family:163 Genus:431 were identified. Bacteria with ROC_AUC greater than 0.65 were TM7 phylum TM7-3 class, Firmicutes phylum Clostridiales class Lachnobacterium, Dialister, Ruminococcus, Roseburia Genus. Firmicutes phylum, and Erysipelotrichi class were found to be a high proportion of the total intestinal flora of cancer patients. The sensitivity and specificity of the combined analysis were 0.76 and 0.75, respectively (P=0.0006).
Conclusion: We investigated the presence of hepatocellular carcinoma and the intestinal microbiota in patients with chronic hepatitis B, and identified several bacteria that are highly prevalent in patients with hepatocellular carcinoma.

P-100
10034

Clinical Feature of Hepatocellular Carcinoma Patients with Overall Survival (10 Years or More)

Takuya Matsuda[1], Atsushi Hiraoka[1], Fujimasa Tada[1], Tomoyuki Ninomiya[1], Yoshiko Nakamura[2], Masashi Hirooka[2], Yoichi Hiasa[2]
[1]Gastroenterology Center, Ehime Prefectural Central Hospital, Ehime, Japan, [2]Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Toon, Japan

Background/Aim: Hepatocellular carcinoma (HCC) patients has been known to be one of malignant disease with poor prognosis. We aimed to elucidate the clinical features of 10-years survival.
Methods: From 2000 to 2013, 845 HCC patients, (median age 69 years, 630 males) were enrolled after excluding drop-out patients. They were divided into before 2007 (Early-group, n=365) and after 2008 (Late-group, n=480). The clinical background of 10-year survivors were evaluated, retrospectively.
Results: The ratio of 10-year survivors (20.0 vs. 14.0%, P=0.02) and overall survival (median 43 vs. 39 months, P=0.01) were better in the Late-group than the other, while 10-year survivors' ratio did not show significant difference between patients treated curatively in both groups (28.4 vs. 24.9%, P=0.41). In patients treated curatively, the 10-year survivors were younger, and showed higher albumin level, platelet count, and prothrombin time, and lower ALBI score (-2.82 vs. -2.48), FIB-4 (3.30 vs. 4.99), AFP (11 vs. 17 ng/mL), PIVKA-II (36 vs. 65 mAU/mL), and TNM classification than the other (each P<0.01). Although the Late-group showed lower HCV patient ratio (63.3 vs. 74.8%), performing rates of anti-HCV treatments (interferon or direct antiviral agents) (50 vs. 6.4%) and SVR (37.5 vs. 3.2%) was higher (each P<0.01) in comparison between 10-year survivors of both groups. In logistic multivariate analysis, ALBI grade 1/2a (OR5.59, P<0.01), SVR (OR17.10, P<0.01), and PS0 (OR4.10, P=0.04) were identified as significant independent factors for 10-year survival.
Conclusion: In HCC patients, good liver function, HCV elimination, and good PS were important factors for long prognosis over 10-years.

P-101
10036

Treatment Outcomes of Patients with Unresectable Hepatocellular Carcinoma: A Single Center Retrospective Cohort Study

Christmae Maxine Solon, Lawrence Liu, Alsalman Anam
Section of Gastroenterology, Department of Internal Medicine, Cebu Doctors' University Hospital, Philippines

Introduction: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer worldwide. This study aims to identify the treatment outcomes of patients with unresectable HCC.
Methodology: 129 patients with unresectable HCC were evaluated at a tertiary hospital in Cebu. Risk factors and treatment outcomes of patients who underwent radiofrequency ablation (RFA), microwave ablation (MWA), transarterial chemoembolization (TACE), systemic chemotherapy and palliative care were evaluated.
Results: The average age at diagnosis was 63.8 years, mostly male. Diabetes mellitus was present in 84.5% of the population. The most prevalent risk factor was hepatitis B. Most cases had BCLC A or B with a well-compensated disease (Child-Pugh A and B). Majority opted for palliative care (46.5%). Only 13.2% underwent chemotherapy while MWA, TACE, RFA were not commonly done (14.0%, 8.5% and 3.1% respectively). Mortality was seen in 18.6% of cases while morbidity was seen in 31.8% of cases. Spontaneous bacterial peritonitis, acute renal failure and septic shock were identified. Disease severity and staging at diagnosis scaled significantly with the proportion of disease morbidity and mortality. Mortality cases were significantly younger with a mean age 57.8.
Conclusion: Chronic hepatitis B is a primary risk factor for the development of HCC. Although diagnosed at earlier stages, most still opt for palliative treatment. This may be due patient's preference, significant comorbidities precluding initiation of treatment and prohibitive cost of available treatment options.

P-102
10048

HBV preS1/HBsAg Ratio is a Predictive Marker for the Occurrence of Hepatocellular Carcinoma

Masanari Kosaka[1], Hatsue Fujino[1], Masataka Tsuge[1,2], Shinsuke Uchikawa[1], Atsushi Ono[1], Eisuke Murakami[1], Tomokazu Kawaoka[1], Daiki Miki[1], C.Nelson Hayes[1,2], Shiro Oka[1]
[1]Department of Gastroenterology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan, [2]Research Center for Hepatology and Gastroenterology, Hiroshima University, Hiroshima, Japan

Aim: The preS1 region, a part of the large hepatitis B virus (HBV) surface protein, plays an important role in HBV infection; however, its effect on the development of hepatocellular carcinoma (HCC) remains unclear. This study investigated the relationship between serum preS1 levels and hepatocarcinogenesis in patients with chronic hepatitis B (CHB).
Methods: We measured preS1 levels in 531 patients with CHB with no history of HCC. Among the 531 patients, 293 HBV carriers who had never received nucleotide/nucleoside analog (NA) therapy had their preS1 levels measured at their first visit (non-NA group), and 238 patients who had received NA therapy had their preS1 levels measured at the start of NA administration (NA group). We analyzed predictors of HCC development in patients with CHB, including preS1 levels.
Results: The two groups had no significant differences in hepatitis B surface antigen (HBsAg) levels; however, the preS1/HBsAg ratio was significantly higher in the NA group. The preS1/HBsAg ratio was significantly different between patients with CHB with high HBV DNA or alanine aminotransferase levels not meeting the NA treatment criteria, and patients with chronic hepatitis and cirrhosis who were eligible for NA treatment. Predictors of HCC development were analyzed and the preS1/HBsAg ratio was identified in the non-NA and NA groups.
Conclusions: The preS1/HBsAg ratio could be a predictor of hepatocarcinogenesis in patients with CHB with or without NA administration. Patients with CHB and a high preS1/HBsAg ratio may have advanced fibrosis and should be considered for antiviral therapy to prevent HCC development.

P-103
10157

Promising Antiviral siRNAs for Targeting NS4A and NS5A in Hepatitis C Virus Genotype 1

Rian Ka Praja[1], Reny Rosalina[2]
[1]Faculty of Medicine, Universitas Palangka Raya, Palangka Raya, Indonesia, [2]Faculty of Mathematics and Natural Sciences, Universitas Palangka Raya, Indonesia

Hepatitis C virus (HCV) infection is recognized as a major global health issue due to its chronic nature and the severe liver complications it causes. The objective of this study was to identify and assess potential antiviral small interfering RNAs (siRNAs) designed to target the NS4A and NS5A proteins of HCV, which are essential for the virus's replication and pathogenicity. Comprehensive bioinformatics tools were utilized to identify and evaluate siRNA candidates capable of effectively silencing NS4A and NS5A of HCV genotype 1. The siPRED tool was used to design siRNA molecules and predict their efficacy with a threshold for inhibition at > 90%. Following this, the siRNA Scales tool was employed to filter the potential candidates. These candidates were then analyzed using MaxExpect to assess the folding free energy of the siRNAs and DuplexFold to determine the binding free energy between the guide strand and the target. A total of 2 siRNAs targeting NS4A and 22 siRNAs targeting NS5A were successfully designed based on the complete genome of HCV genotype 1 (NC_004102.1). Further analysis with various bioinformatics tools identified siRNAs with high potential for silencing NS4A and NS5A, achieving efficacy levels of 93.14% and 94.68%, respectively. In conclusion, promising siRNA molecules were introduced as potential candidates for antiviral therapy targeting HCV genotype 1. However, laboratory validation of these predicted siRNAs remains essential for confirming their effectiveness.

P-104
10162

The Correlation between Interleukin-6 and the Progression of Chronic Hepatitis B

Mohamed Shafi Mahboob Ali
Ministry of Higher Education of Malaysia

Background: Hepatitis B virus (HBV) is a dreadful virus with the potential to cause human liver diseases such as chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC). Cytokines have been shown to be engaged in regulating hepatocyte functions, and play an important role in HBV infection immunopathogenesis.
Methods: About 52 subjects ranging from 18 years old to 80 years old who were diagnosed with HBV were recruited into the studies. The patient's sera were withdrawn and divided into two aliquots. The first group of sera were subjected to a hybrid capture, while the second group of sera were subjected to a sandwich-ELISA test using LEGEND MAX Deluxe set human IL-6 kit to quantify the IL-6 levels.
Results: The more severe the infection, the higher the IL-6 level($P<0.05$) taking the mean value of IL-6 as 132.6pg/ml. A linear scatter plot was derived between the levels of IL-6 and HBV viral load. Pearson correlation coefficient showed a linear correlation between the two variables. The patient's ALT enzyme was used to stratify the severity of the liver functions. Higher levels of IL-6 were detected in the subjects with HBV for longer than 6 months which proved that IL-6 levels correspond to the chronicity of the disease.
Conclusion: Our studies proved that serum IL-6 levels were positively correlated with HBV disease severity and chronicity. Thus, IL-6 may be a useful indicator of disease activity and therapeutic efficacy in patients suffering from hepatitis B.

P-105
10142

An Advanced Predictive System Using Gradient Boosting Machines (GBM) to Forecast Hepatocellular Carcinoma in Patients with Chronic Hepatitis C Virus Infection

Prihantini Prihantini[1], Rifaldy Fajar[2], Sahnaz Vivinda Putri[3], Andi Nursanti Andi Ureng[4]
[1]Machine Learning for medicine Laboratory, Bandung Institute of Technology, Indonesia, [2]Computational Biology and Medicine Laboratory, Yogyakarta State University, Indonesia, [3]General Surgery Research Division, Daeng Radja Hospital, Indonesia, [4]Department of Pharmacy, Andini Persada College of Health Sciences, Indonesia

Gradient Boosting Machines (GBM) have revolutionised predictive modelling in healthcare. Leveraging GBM to forecast hepatocellular carcinoma (HCC) development in chronic hepatitis C virus (HCV) patients addresses a significant risk factor for HCC, requiring accurate tools for early intervention. The GBM model integrates liver function tests, viral load, demographic data, and treatment history to enhance prediction accuracy. By analysing longitudinal patient data, it identifies critical predictors and HCC progression patterns, supporting proactive medical strategies. Validation through rigorous comparison with statistical methods underscores its predictive accuracy and clinical relevance, aiming to establish a robust framework for HCC risk assessment in chronic HCV patients, thus advancing personalised medicine and improving outcomes. A comprehensive dataset of clinical, demographic, and treatment-related variables from chronic HCV patients was utilised. The GBM model was developed with pre-processing steps by handling missing values, normalisation, and feature selection. Data were split into training and testing sets, with cross-validation ensuring robustness. Hyper-parameter tuning via grid search optimised predictive accuracy. Performance was assessed using metrics like AUC-ROC, precision, recall, and F1 score, and compared to traditional predictive models. Results showed the GBM model's superior performance in predicting HCC, achieving an AUC-ROC of 0.92, precision of 0.87 and recall of 0.85. Feature importance analysis identified liver function tests, viral load, and age as key predictors. Consistent performance across patient subgroups was confirmed by cross-validation. The GBM model, integrating diverse variables, enhances early detection treatment strategies, improving clinical outcomes in chronic HCV care and potential to revolutionise predictive modelling in healthcare.

P-106
10103

A Case of Atezolizumab-Bevacizumab Combination Therapy with Good Long-Term Prognosis Despite Prolonged Bevacizumab Withdrawal

Fumiya Suzuki, Hiroaki Haga, Fumi Uchiyama, Keita Maki, Tomohiro Katsumi, Kyoko Hoshikawa, Yoshiyuki Ueno
Department of Gastroenterology, Yamagata University Faculty of Medicine, Japan

Background: Bevacizumab inhibits angiogenesis, tumor growth, and metastasis by blocking vascular endothelial growth factor (VEGF). However, patients experiencing proteinuria, a side effect of bevacizumab, may need to switch to atezolizumab monotherapy after discontinuing bevacizumab. In this study, we report a case where a good long-term prognosis was achieved even after the long-term withdrawal of bevacizumab in combination therapy with atezolizumab and bevacizumab(Atez/Bev), with a discussion of the relevant literature.
Case Description: A 72-year-old man had undergone multiple radiofrequency ablations (RFA) for segment 8 hepatocellular carcinoma (S8HCC) with a background of type C cirrhosis from 2014 to 2017. In August 2017, a CT scan revealed multiple masses at the right hepatic lobe margins, leading to the introduction of sorafenib. In May 2018, he was switched to regorafenib. Although the S8 lesion remained small, other lesions were generally increasing, so Atez/Bev was initiated in February 2021. After 12 courses, proteinuria was observed, leading to a switch to atezolizumab monotherapy. He is currently on the 35th course, with all intrahepatic lesions maintained at a reduced size. However, the lymph nodes near the superior mesenteric artery and inferior vena cava have gradually enlarged, leading to the addition of radiotherapy in December 2023. Both lymph nodes have maintained their size since then.
Discussion: Monotherapy with atezolizumab alone can only inhibit the PD-1/PD-L1 pathway and has limited therapeutic effect. However, multimodality treatment may stimulate the release of cancer antigens, and, as in this case, atezolizumab alone may have a therapeutic effect.

P-107
10134

A Case of Hepatocellular Carcinoma with Bone Metastasis Achieved Complete Response Using Stereotactic Radiotherapy and Lenvatinib, Following Anti-PD-L1 Antibody-induced Psoriasis-like Dermatitis

Chikako Nagao, Masanori Atsukawa, Taeang Arai, Tadamichi Kawano, Michika Kitamura, Kaori Koyano, Yuta Hasegawa, Norio Itokawa, Keiko Kaneko, Katsuhiko Iwakiri
Division of Gastroenterology and Hepatology, Nippon Medical School, Tokyo, Japan

Bone metastases from hepatocellular carcinoma (HCC) severely worsen quality of life and prognosis, and their control is often challenging. We report a case of anti-PD-L1 antibody-induced psoriasis-like dermatitis following Atezolizumab/bevacizumab (Atz/Bev) therapy for postoperative bone metastasis of HCC, and successfully achieved complete response to lenvatinib (LEN) with sequential stereotactic radiotherapy (SRT). The patient, a male in his 50s with MASLD, had previously undergone a right hepatic lobectomy for a 12 cm HCC in the right lobe and was diagnosed with pT3N0M0, Stage III (intermediate differentiated HCC). Subsequently, a suspected metastatic bone tumor was identified in the second lumbar vertebra. A CT-guided needle biopsy confirmed the diagnosis of recurrent bone metastasis. Although Atz/Bev therapy was initiated, the patient developed grade 3 psoriasis-like dermatitis induced by the anti-PD-L1 antibody after the second course, necessitating discontinuation of the treatment. Following SRT (20Gy/1Fr), LEN therapy was initiated and maintained, resulting in a complete response observed 30 months post-initiation. The psoriasis-like dermatitis improved with the discontinuation of Atz/Bev and phototherapy, with further improvement noted after switching to LEN. In cases of bone metastasis, intrahepatic control of HCC is significantly associated with prognosis. The favorable treatment outcome in this case is thought to have been achieved through effective SRT and systemic chemotherapy, supported by good control of intrahepatic lesions. Regarding psoriasis-like dermatitis, lenvatinib likely improved the condition by inhibiting vascular endothelial growth factor, a known trigger for the onset and exacerbation of psoriasis, in addition to the discontinuation of Atz/Bev and phototherapy.

Poster Session

P-108
10146

A Case of Hepatocellular Carcinoma with Multiple Pulmonary Metastatic Recurrences at Distant Stage after Radical Cure

Akihiko Nishimura, Akio Moriya
Department of Gastroenterology, Mitoyo Jeneral Hospital, Kagawa, Japan

The patient was a 60-year-old woman with hepatocellular carcinoma at the time of initial presentation. She was aware of swelling in the right side of the abdomen and visited her local doctor, who pointed out a hepatic mass and referred her to our hospital in X year. Blood test showed a high level of PIVKA-II 20400 mAU/mL, and abdominal CT and EOB-MRI showed an 8.2 x 7.2 cm mass in the right lobe of the liver. In X+2, TACE and RFA were performed for a 15 mm-sized HCC in S1-4. In X+3, Lip-TACE and RFA were performed for a 10 mm-sized and 5 mm-sized tumor in the vicinity of the sub-dome. Thereafter, the patient had no recurrence or metastatic findings, but a CT scan of the chest and abdomen in X+14 revealed multiple nodules in both lungs that had not been detected in the previous year. Lung tumor biopsy diagnosed lung metastases of hepatocellular carcinoma. Blood tests at this time showed a re-elevation of PIVKA-II 111.0 mAU/mL. Atezolizumab plus bevacizumab combination therapy was administrated, and the nodule shadow gradually shrank and CR was obtained. Due to adverse events, the treatment was terminated after 15 courses, but at 1 year and 4 months after the end of the treatment, the patient was still drug free and maintained CR.

P-109
10147

Remarkable Response to Atezolizumab plus Bevacizumab Therapy after Psuedo-progression, Followed by Phenotypic Change in Conversion Surgery: A Unique Case of Hepatocellular Carcinoma

Midori Sawada, Sadahisa Ogasawara, Makoto Fujiya, Takahiro Tsuchiya, Teppei Akatsuka, Ryo Izai, Chihiro Miwa, Takuya Yonemoto, Sae Yumita, Ryuta Kojima, Hiroaki Kanzaki, Keisuke Koroki, Masanori Inoue, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Shingo Nakamoto, Naoya Kato
Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

Introduction: Pseudo-progression induced by immune-checkpoint inhibitors (ICIs) is sometimes difficult to diagnose. The comparison of pathological finding of original and recurrent tumor is not always available.
Case: A 55-year-old male underwent a posterior sectionectomy for hepatocellular carcinoma (HCC), pathologically diagnosed as moderately differentiated HCC. Although he began nucleotide analog therapy for untreated hepatitis B postoperatively, intrahepatic multifocal recurrence of HCC was observed a year later, without vascular invasion but with lung metastasis. Following initiation of Atezolizumab plus Bevacizumab (Atez/Bev), six-week imaging revealed enlarged intrahepatic lesions, while AFP levels spiked from 569.1 to 1438.4 ng/mL within three weeks, suggesting progression. However, at the eight-week mark, AFP levels decreased and tumors began to shrink. This reversal confirmed that the initial enlargement was pseudo-progression. Atez/Bev therapy ultimately proved highly effective. After eight courses of Atez/Bev, AFP levels normalized, and almost all tumors disappeared, except for a persistent 75 mm nodule in segment 8 of the liver. After thorough consultation, hepatic resection was performed following 15 courses of Atez/Bev therapy. This approach enabled him to achieve cancer-free status and remain recurrence-free for 25 months. Interestingly, the pathology of the second resected tumor was completely different from the first, presenting as a biphasic tumor with mesenchymal and epithelial components, exhibiting characteristics reminiscent of blastoma or seminoma.
Discussion: During ICI treatment, pseudo-progression can occur, making evaluation with criteria such as irRECIST, along with blood biomarkers, essential. The pathological change indicates that the remaining tumor may have persisted due to immune escape from Atez/Bev therapy.

P-110
10169

A Cholangiolocellular Carcinoma Case Showing Slow Tumor Growth and Marked Intratumoral Lymphocyte Infiltration, with a Favorable Outcome

Ayaka Gamo[1], Akiko Saito[1], Yasuo Tanaka[1], Mikio Yanase[1], Fuyuki Inagaki[1], Norihiro Kokudo[1], Hidemiki Miyazaki[1], Masayuki Nakano[2]
[1]National Center for Global Health and Medicine, [2]Tokyo Central Pathology Laboratory

Patient: A 76-year-old male, with an irregular hypoechoic mass incidentally detected on US, underwent contrast-enhanced US which revealed arterial whole-tumor enhancement, and washout within one minute. The mass (46 mm) showed arterial phase peripheral enhancement and equilibrium phase delayed enhancement on CECT. Retrospectively, the mass had first appeared as a 6-mm arterio-portal shunt 9 years earlier. The tumor doubling time (DT) was 380 days. EOB-MRI showed decreased uptake in the hepatobiliary phase. HBV and HCV were both negative. CA 19-9 was 43.7 U/mL. As intrahepatic cholangiocarcinoma (ICC) or cholangiolocellular carcinoma (CoCC) was suspected, partial hepatectomy was performed. A small tubular structure with apical membranes positive for EMA staining on microscopy yielded a CoCC diagnosis. Intratumoral lymphocyte infiltration was prominent. Focal lymphocyte infiltration in the portal tract was observed in the surrounding liver parenchyma but there was no fibrosis. He has remained recurrence-free for 2 years postoperatively.
Discussion: CoCC is included among small duct ICC according to the 2019 WHO classification. Our CoCC patient had the longest elapsed time among reported cases with ICC or CoCC. DT was prolonged as compared to previously reported DT (median: 70 days) in ICC cases, implying a good outcome. Like lymphocyte-rich HCC, marked intratumoral lymphocyte infiltration may correlate with slow tumor growth and good outcomes.
Conclusion: The relationship between intratumoral lymphocyte infiltration and clinical features merits meticulous diagnostic studies with more cases.

P-111
10001

Survey of Systemic Drug Therapy for Unresectable Hepatocellular Carcinoma in Non-designated Regional Cancer Treatment Hospital in Japan

Hidehiro Kamezaki, Daiki Takahashi, Kenta Tada, Wei Yang, Terunao Iwanaga, Takahiro Maeda, Junichi Senoo
Department of Gastroenterology, Eastern Chiba Medical Center, Togane, Japan

Backgrounds: We investigate the actual status of systemic drug therapy for unresectable hepatocellular carcinoma in our hospital, which is not designated regional cancer treatment hospitals in Japan.
Methods: We selected cases in which systemic drug therapy was introduced for unresectable hepatocellular carcinoma by September 2023 at our hospital, and divided into two groups: those with a regimen including immune checkpoint inhibitors (ICI group) and not including (non-ICI group).
Results: Patients were classified into 11 ICI group (11 atezolizumab/bevacizumab) and 22 non-ICI group (12 sorafenib and 10 lenvatinib). Median age was 73 vs. 72 years, 90.9% vs. 95.5% male, 72.7% vs. 77.3% with prior treatment, 54.5% vs. 59.1% with viral hepatitis, median AFP (ng/mL) was 29.0 vs. 585.4, and the Child-Pugh A was 72.7% vs. 54.5%, all without significant differences. The disease control rate was 88.9% vs. 64.7%, and the overall response rate was 66.7% vs. 35.3%, which did not reach significance but tended to be better in the ICI group. Among Child A patients, the 1-year survival rate was 75.0% vs. 41.7%, the 2-year survival rate was 60.0% vs. 31.3%, and those who received second-line treatment was 75.0% vs. 50.0%, a trend toward higher rates in the ICI group. The rate of treatment discontinuation due to adverse events was 0% vs. 36.4% (P=0.031), with a higher rate in the non-ICI group.
Conclusion: The treatment of unresectable hepatocellular carcinoma has improved with the advent of ICI, even in our hospital, which is not designated regional cancer treatment hospital in Japan.

P-112
10044

Hepatic Dysfunction in 879 ICI-treated Patients; Does Referral to a Hepatologist Improve OS?

Kaori Matsumoto[1], Tatsuo Kanda[2], Masao Omata[3]
[1]Department of Pharmacy, Yamanashi Prefectural Central Hospital,Yamanashi,Japan, [2]Division of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, [3]The University of Tokyo, Japan

Aim: Hepatic injury, an immune-related adverse event (irAE) caused by immune checkpoint inhibitor (ICI) therapy, is often diagnosed by the attending physician, but not often referral to hepatologist. The aim of this study was to investigate whether the specialist referral influence outcome of patients with hepatic injury(irAE).
Methods: We investigated the occurrence of irAE in 879 patients treated with ICI between November 2014 and December 2024, and compared OS with and without continuation of treatment due to various including irAE hepatic injury type.
Results: Of 879 patients treated with ICI, 325 (37%) developed irAE of all kinds, including 53 (6.0%) hepatic injury. Of these 53, 26 patients continued ICI treatment overcoming injury, whereas 27 discontinued. We, hepatologists, further studied the details of liver function tests in retrospect. Of 27 discontinued patients, 20 (38%) had Grade 3/4 ALT/AST elevations, but only 3 (11%) had T-Bil Grade 3 (≥4.5 mg/dL), and 7(26%) had prolonged prothrombin time (≥14 seconds), a possible sign of impending hepatic failure. Of 53 with hepatic irAE, median OS was 54.3 months in the continuation group (n=26) and 26.2 months in the discontinuation group (n=27) (P=0.142).
Conclusion: Most patients who developed hepatic injury stopped ICI, because of elevated transaminases, but without stigmata of impending hepatic failure. Referral to a hepatologist for a comprehensive evaluation of impending hepatic failure, including prothrombin time, may contribute to continued ICI treatment and thus prolong the patient's life expectancy.
As a reference, the median OS for all irAE-expressing groups (n=325) was 34.2 months, and 13.1 months for non-expressing groups (n=554) (P<0.001).

P-113
10061

Atezolizumab plus Bevacizumab Shows PFS Benefit in mALBI Grade 2 HCC

Shunji Watanabe, Yosuke Otsuka, Wataru Ueno, Hiroshi Maeda, Rie Goka, Yoshinari Takaoka, Hiroaki Nomoto, Mamiko Tsukui, Kouichi Miura, Naoki Morimoto
Department of Medicine, Division of Gastroenterology, Jichi Medical University, Tochigi, Japan

Background and Objectives: Atezolizumab plus Bevacizumab (ATZBV) therapy has shown favorable outcomes. However, the IMbrave150 trial required Child-Pugh (CP) Class A, while real-world cases often have reduced liver function. This study examines the efficacy and related factors of ATZBV in patients with varying liver function at our institution.
Methods and Results: From October 2020 to December 2023, 134 advanced hepatocellular carcinoma (HCC) cases were treated with ATZBV at our institution. We assessed objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and their relation to background factors. The patient background included a median age of 73 years, with 108 males (80.6%). CP Class were A in 99 cases, B or C in 35 cases. According to mALBI grade(Gr), there were 39 cases in Gr1, 30 in Gr2a, 55 in Gr2b, and 10 in Gr3. ORR and DCR were 30.6% and 79.8%, respectively. Multivariate analysis identified CP Class and mALBI grade as factors contributing to PFS and OS, with macroscopic vascular invasion (MVI) also impacting OS. There was no difference in PFS and OS among the mALBI Gr1, 2a, and 2b groups (Median PFS/Median Survival Time (MST): 1: 18.6 months (M)/not reached, 2a: 8.6M/20.8M, 2b: 9.4M/15.9M), but mALBI grade 3 (3.8M/5.4M) showed significant (p=0.0015) shortening.
Discussion: Compared to the IMbrave150 trial, our study showed better results for patients up to mALBI grade 2b or CP score 8. Thus, ATZBV therapy could be acceptable in real-world practice. Liver function, including serum albumin levels, is crucial in treatment selection.

P-114
10075

Results of Atezolizumab Combined with Bevacizumab for Advanced Hepatocellular Carcinoma in Vietnamese Patients

Hang Thu Hoang, Tuan Anh Pham
On-demand Treatment Department, National Cancer Hospital Vietnam

Backgrounds: Atezolizumab plus bevacizumab (AB) was approved in 2022 in Vietnam as a first-line treatment for advanced hepatocellular carcinoma (aHCC). The purpose of this study was to assess the effect and tolerability of the immuno-targeted combination treatment in aHCC.
Methods: Retrospective study, single-arm, single center on 31 patients diagnosed with aHCC defined as the Barcelona clinic liver cancer staging system (BCLC) stage B was unsuitable or failed with local interventions or BCLC stage C, indicated systemic therapy with AB regimen at National Cancer Hospital Vietnam between 2022 and 2023.The outcomes included overall response (OR), median overall survival (mOS), median progression-free survival (mPFS), and adverse events (AEs).
Results: The response rate was 41.9%, mPFS was 5 months and mOS was 15.5 months. Grade 3 and 4 toxicities occurred in 9.7% patients including hypertension, increased liver enzymes and thrombocytopenia.Twenty-three studies, comprising 3168 patients, were enrolled. The pooled OR, CR, and PR rates of the long-term (more than six weeks) therapy response based on Response Evaluation Criteria in Solid Tumors (RECIST) were 26%, 2%, and 23%, respectively. The pooled OR, CR, and PR rates of the short-term (six weeks) therapeutic response evaluated with RECIST were 13%, 0%, and 15%, respectively. The pooled mOS and mPFS were 14.7 months and 6.66 months, respectively. During the treatment, 83% and 30% of patients experienced any grade AEs and grade 3 and above AEs, respectively.
Conclusions: Bevacizumab-Atezolizumab regimen is effective and well-tolerated in patients with aHCC in Vietnam.

P-115
10099

Assessment of Macrovascular Invasion in Advanced Hepatocellular Carcinoma: Clinical Implications and Treatment Outcomes with Systemic Therapy

Masanori Inoue[1], Sadahisa Ogasawara[1], Tomomi Okubo[2], Norio Itokawa[2], Masamichi Obu[4], Keisuke Koroki[1], Masato Nakamura[1], Naoya Kanogawa[1], Takayuki Kondo[1], Shingo Nakamoto[1], Kengo Nagashima[5], Ei Itobayashi[6], Masanori Atsukawa[2,3], Yoshihiro Koma[4], Ryosaku Azemoto[4], Naoya Kato[1]
[1]Department of Gastroenterology, Graduate School of Medicine, Chiba University, [2]Nippon Medical School Chibahokusoh Hospital, [3]Nippon Medical School, [4]Kimitsu Chuo Hospital, [5]Clinical and Translational Research Center, Keio University Hospital, [6]Asahi General Hospital, Japan

Background and Aims: Macrovascular invasion (MVI) is a strong prognostic factor for advanced hepatocellular carcinoma (HCC). However, it is difficult to objectively evaluate MVI progression, using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1). We standardized the MVI assessment and validated its clinical relevance.
Methods: We collected clinical data from patients with advanced HCC with MVI undergoing first-line systemic therapy at four medical centers in Japan. We used Macrovascular Invasion Progressive Disease (MVI-PD) to monitor MVI progression, and RECIST v1.1-PD to assess tumor enlargement and new lesions. We evaluated the prognostic impact of the MVI-PD and RECIST v1.1-PD.
Results: Of the 189 patients, 95 (50.3%) were diagnosed with MVI-PD during the entire first-line treatment period and 85 were confirmed to have MVI-PD within 3 months of starting treatment initiation. In the landmark analysis of overall survival (OS), patients without concurrent MVI-PD and RECIST v1.1-PD during the initial 3 months had the longest median OS of 19.7 months, while those with both had the shortest at 5.4 months. For patients with only RECIST v1.1-PD or MVI-PD occurring within 3 months, OS was 7.2 months and 7.4 months, respectively ($p<0.001$). The correlation coefficients between PFS and OS were similar for MVI-PD (0.515) and RECIST v1.1-PD (0.498).
Conclusions: MVI progression during systemic therapy for advanced HCC with MVI appears to be strongly associated with poor OS. To evaluate the efficacy of systemic therapy for HCC with MVI, it is necessary to assess MVI progression.

P-116
10107

A Retrospective Analysis of Liver Volume Decrease in Advanced Hepatocellular Carcinoma Patients Treated with Atezolizumab plus Bevacizumab and Lenvatinib

Tomoharu Yamada, Taijiro Wake, Makoto Moriyama, Yuki Matsushita, Kazuya Okushin, Takuma Nakatsuka, Masaya Sato, Tatsuya Minami, Mitsuhiro Fujishiro, Ryosuke Tateishi
Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Background: In the treatment of advanced hepatocellular carcinoma (HCC), multi-kinase inhibitors with anti-vascular endothelial growth factor (VEGF) activity, and anti-VEGF monoclonal antibodies in combination with immune checkpoint inhibitors, are available options. The aim of this study is to investigate the serial changes in liver volume in patients treated with atezolizumab plus bevacizumab (Atezo/Bev) and those treated with lenvatinib.
Methods: Patients receiving Atezo/Bev or lenvatinib as a first-line treatment for advanced HCC from October 2018 to May 2023 were included. Liver volume was measured at baseline, 8, and 16 weeks. Linear regression analysis was used to evaluate the factors associated with changes in liver volume.
Results: Seventy-three patients (40 Atezo/Bev, 33 lenvatinib) were included. Liver volume decreased in 54 patients (74%) at week 8; the average volume relative to baseline was 0.92 (95% CI: 0.90-0.94, $p < 0.01$). Liver volume decreased in both those with shrinking tumors and those with enlarged tumors. Multivariable logistic regression showed that the decrease in liver volume was more pronounced in the lenvatinib group than in the Atezo/Bev group ($p = 0.04$).
Conclusions: Anti-angiogenic therapy for advanced HCC may cause liver atrophy.

P-117
10121

Diagnosis Triggers and Outcomes in Patients Treated with Atezolizumab/Bevacizumab as Initial Treatment for Hepatocellular Carcinoma

Teiji Kuzuya, Naoto Kawabe, Yoshiki Hirooka
Department of Gastroenterology and Hepatology, Fujita Health University, Aichi, Japan

Objective: The incidence of hepatocellular carcinoma (HCC) associated with metabolic diseases such as diabetes and fatty liver is increasing. These patients often miss early HCC screening, leading to advanced stage diagnoses unsuitable for local treatment. This study examines the triggers of HCC diagnosis, clinical characteristics, and outcomes in patients receiving atezolizumab plus bevacizumab (Atz/Bev) as initial treatment for HCC.
Methods: From October 2020 to May 2024, 96 patients treated with Atz/Bev as first-line systemic therapy were studied. They were divided into two groups: 48 with no previous HCC treatment (initial HCC group) and 48 with previous HCC treatment (non-initial HCC group). Clinical characteristics and outcomes were compared.
Results: The initial HCC group had a higher proportion of males, larger tumors (more than 50mm), greater liver involvement (more than 50%), and higher DCP levels than the non-initial HCC group. Better progression-free survival (PFS) was associated with non-viral HCC, absence of portal vein tumor thrombosis and being in the initial HCC group. In the initial HCC group, 68.7% were asymptomatic at diagnosis and 58.3% were seeking medical care for other conditions. Most were diagnosed by imaging for mild liver dysfunction during treatment for diabetes or hypertension.
Conclusions: Patients treated with Atz/Bev as initial HCC therapy had relatively good outcomes despite higher tumor volumes compared to those with prior treatment. The importance of early screening for HCC in patients with diabetes and coexisting fatty liver was reaffirmed.

P-118
10027

Systemic Therapy for Unresectable HCC Combination with TACE (Lenvatinib or Atezolizumab/Bevacizumab)

Ryu Sasaki, Yasuhiko Nakao, Masanori Fukushima, Masafumi Haraguchi, Satoshi Miuma, Hisamitsu Miyaaki
Department of Gastroenterology and Hepatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Background: The combination of locoregional therapy is useful in systemic therapy for unresectable HCC. There have been several reports of therapeutic efficacy of Lenvatinib(LEN)-TACE therapy. In clinical practice, TACE combination is also performed in the current first-line Atezolizumab/Bevacizumab (A/B). In this study, we retrospectively compared the treatment outcomes of LEN-TACE and A/B-TACE.
Methods: Among 301 patients who underwent LEN for uHCC at our facilities, 57 patients were treated with TACE, and among 157 patients who underwent A/B, 12 patients were treated with TACE. Treatment efficacy was evaluated based on RECIST ver1.1.
Results: 57 patients underwent LEN-TACE therapy [median age 72.0 years, 48 males, 33 BCLC stage B], and 12 patients underwent A/B-TACE [median age 70.0 years, 8 males, 6 BCLC stage B], with no significant difference in background factors. The treatment effect was OR 16.0%, DC 81.7% in the LEN-TACE and OR 8.3%, DC 75.0% in the A/B-TACE. MST was 24.3 months in the LEN-TACE and 26.9 months in the A/B-TACE ($p = 0.763$), with no significant difference. Adverse events such as HFS, fatigue, hypertension, and decreased appetite tended to occur more frequently in the LEN-TACE. In addition, adverse events of grade 3 or higher tended to occur more frequently in the A/B-TACE.
Conclusions: No significant difference in treatment outcomes was observed between LEN-TACE and A/B-TACE. The tolerability of TACE combination therapy seemed to depend on the tolerability of the drugs, but it was also suggested that the timing and reasons for TACE combination therapy may differ between LEN and A/B.

P-119
10100

Efficacy of Lenvatinib + New FP Combination Therapy in the Treatment of Unresectable Advanced Hepatocellular Carcinoma

Susumu Maruta[1], Yohei Koshima[1], Taro Watabe[1], Ryo Tamura[1], Masanori Takahashi[1], Tadashi Ohshima[1], Yoshihiko Ooka[2], Ryo Chinzei[1], Takehiro Yoshii[1], Keisuke Watanabe[1], Hideto Imai[1], Satoru Ishida[1], Yuuho Morita[1]
[1]Department of Gastroenterology, Saitama Red Cross Hospital, Saitama, Japan, [2]Chiba Chuo Clinic, Japan

A man in his 50s was diagnosed with advanced hepatocellular carcinoma in December X, for which atezolizumab+bevacizumab therapy was administered. In July X+1, the patient was diagnosed with Progressie Disease(PD). Therefore, we started New FP monotherapy. However, after two courses, he was diagnosed with PD. In September X+1, the third course was combined with lenvatinib (LEN-NewFP). In December X+1, the contrast enhancement effect in the target lesion decreased and the tumor size decreased. In February X+2, intrahepatic lesions were well controlled and no viable tumor was found within the liver, but new lung metastases were observed. The patient was therefore diagnosed with PD and switched to other treatments. Patients with advanced hepatocellular carcinoma undergo LEN-NewFP therapy, which showed excellent results. Even with the remarkable development of systemic chemotherapy for advanced HCC, LEN-NewFP has the potential to be a breakthrough therapy with appropriate case selection.

P-120
10124

Combining On-demand Locoregional Treatment for Drug-resistant Lesions during Atezolizumab and Bevacizumab Therapy in Unresectable Hepatocellular Carcinoma

Tasuku Nakabori, Kaori Mukai, Masaki Kawabata
Department of Hepatobiliary and Pancreatic Oncology, Osaka International Cancer Institute, Osaka, Japan

Background: Because appearance of drug-resistant lesions (enlargement of existing lesions or new lesions) during systemic chemotherapy is judged as progressive disease (PD), the treatment regimen is changed. On the other hand, locoregional treatment (LRT) is expected to enhance the therapeutic effect of immunotherapy via activating the host immune response following immunogenic cell death. Thus, we investigated feasibility of combining on-demand LRT for drug-resistant lesions during Atezo/Bev in unresectable HCC.
Methods: We retrospectively analyzed unresectable HCC cases in which Atezo/Bev was administered as first-line treatment.
Results: In the LRT combination group (n=10), 8 RFAs and 5 SBRTs were performed. The median Atezo/Bev withdrawal duration due to LRT was 49 days. The control group consists of PD cases with Atezo/Bev alone (n=26). There were no significant differences in the hepatic reserve and tumor-related factors at the Atezo/Bev initiation between the two groups. The median PFS of Atezo/bev of the combination group (22.0 months) was longer than not only that of the control group (6.6 months) but also the median time to second-line PD in the control group (11.3 months). The median OS of the combination group (32.8 months) was longer than that of the control group (15.9 months). In the combination group, deterioration of disease due to Atezo/Bev interruption was not observed, and the ALBI score did not change after the LRT. No serious complications due to LRT occurred.
Conclusions: Combining on-demand LRT for drug-resistant lesions during Atezo/Bev could be a treatment option, if safely performed without reducing hepatic reserve.

P-121
10138

Effectiveness of Immune Checkpoint Inhibitor Therapy with Locoregional Therapy Versus ICI Alone in Unresectable Hepatocellular Carcinoma: A Retrospective Analysis

Yasuhide Motoyoshi, Masaki Nakamura, Tomohito Kojima, Yuki Kugiyama, Tomoyuki Suehiro, Akira Saeki, Shinya Nagaoka, Kazumi Yamasaki, Atsumasa Komori, Hiroshi Yatsuhashi
National Hospital Organization (NHO) Nagasaki Medical Center, Department of Hepatology, Japan

Objective: In Japan, atezolizumab + bevacizumab and durvalumab + tremelimumab are used for the treatment of unresectable hepatocellular carcinoma (HCC). Given evidence suggesting that combining immune checkpoint inhibitors (ICIs) with locoregional therapies can enhance treatment efficacy, this study retrospectively investigated the combined effect of ICI therapy and locoregional therapy at our hospital.
Methods: We included 34 patients who started ICI therapy at our hospital between December 2020 and March 2024 and received at least two courses of treatment. Among them, 10 patients (Group A) received locoregional therapy within 3 months before or during ICI therapy, while the control group (Group B) consisted of 24 patients who received ICI therapy alone. The primary endpoint was progression-free survival (PFS), and the secondary endpoint was overall survival (OS). We compared these endpoints between the two groups.
Results: No significant differences were found in baseline characteristics between the two groups, although Group B had a significantly higher incidence of extrahepatic metastases ($P = 0.003$). Regarding the primary endpoint, the median PFS was 671 days for Group A and 212 days for Group B ($P = 0.034$, log-rank test). For the secondary endpoint, the median OS was not reached for Group A and 429 days for Group B ($P = 0.030$, log-rank test).
Conclusion: Locoregional therapy administered before or during ICI therapy may extend treatment duration and improve survival in patients with unresectable HCC.

P-122
10149

Is Lenvatinib Resumption Necessary after Lenvatinib-TACE Combination Treatment?

Rie Sugimoto, Yoshihiko Shibata, Yusuke Morita, Yuki Tanaka
Department of Hepato-Biliary-Pancreatology NHO Kyushu Cancer Center Fukuoka, Japan

Background: The benefit of Lenvatinib (LEN)-TACE in intermediated hepatocellular carcinoma is widely recognized. It has been reported that 100% relative volume intensity (RDI) of LEN before TACE is necessary for therapeutic efficacy in this treatment, but that the relative volume intensity of LEN after TACE does not correlate with therapeutic efficacy. However, VEGF is thought to be elevated by the ischaemic state after TACE, and some believe that inhibition of this by LEN may contribute to survival.
Objective: To assess the usefulness of LEN resumption in LEN-TACE therapy. METHODS; We retrospectively investigated differences in efficacy, safety, treatment efficacy, progression-free survival (PFS) and Overall survival(OS) with and without LEN resumption after TACE in 33 patients who underwent LEN-TACE at our institution.
Results: Of the 33 patients, 14 were restarted on LEN after TACE and 19 were not. Resumption or not was left to the patient's wishes and the decision of the attending physician. There were more pre-treatment TACE cycles in the no LEN re-administration group, but otherwise no significant differences. The median PFS by RECIST was 17.0 months in the with re-administration group and 10.6 months in the without re-administration group, a significant difference (p=0.0362); OS was 36.5 months in the with re-administration group and 28.2 months in the without re-administration group, with a trend towards longer OS in the with re-administration group.
Conclusions: In LEN-TACE treatment, the resumption of even small doses of LEN after TACE may lead to improved prognosis.

P-123
10165

Effect of Radiofrequency Ablation on the Therapeutic Efficacy of Atezolizumab/Bevacizumab Combination Therapy

Masahiko Tameda, Hideaki Tanaka, Hayato Nakagawa
Department of Gastroenterology and Hepatology, Mie University Hospital, Mie, Japan

Objective: Immune checkpoint inhibitors (ICIs) are increasingly used as first-line treatment for unresectable hepatocellular carcinoma (HCC), but factors influencing the immune response remain poorly understood. This study investigates the relationship between prior treatments and outcomes in patients treated with the combination of atezolizumab and bevacizumab (Atezo/Bev).
Methods: Patients with unresectable HCC who received Atezo/Bev at our institution between October 2020 and July 2023 and who had received prior therapy within two years before the start of Atezo/Bev were included.
Results: Forty-five patients were enrolled. The best responses were CR in 4 cases, PR in 7 cases, SD in 21 cases, and PD in 10 cases, resulting in a response rate of 24.4%. Sixteen patients had received RFA, 27 TACE, and 15 surgical resection. Response rates were 33.3% for patients who received RFA, 25.9% for TACE, and 20.0% for surgical resection. In the subgroup of 9 patients who underwent RFA within one year before starting Atezo/Bev, the best responses were CR in 4 cases, PR in 1 case, SD in 2 cases, and PD in 2 cases, with a significantly better response rate of 55.6%. There were no significant differences in background characteristics between the two groups.
Conclusion: Patients who underwent RFA within one year before starting Atezo/Bev therapy had a significantly higher response rate than those who did not undergo RFA. These results suggest that RFA performed before Atezo/Bev therapy may influence the immune response to ICIs.

P-124
10029

Carbon-ion Radiotherapy for Hepatocellular Carcinoma 4 cm or Larger

Tetsuro Isozaki[1], Masaru Wakatsuki[1], Makoto Shinoto[1], Shigeo Yasuda[1,2], Hirokazu Makishima[1,3], Shigeru Yamada[1], Hirotoshi Takiyama[1], Yukiko Yamaguchi[1], Hiroki Kurosaki[1], Hitoshi Ishikawa[1]
[1]National Institutes for Quantum Science and Technology QST Hospital, Chiba, Japan, [2]Department of Radiology, Chiba Rosai Hospital, Chiba, Japan, [3]Department of Radiation Oncology, University of Tsukuba Hospital, Tsukuba, Japan

Background: Carbon-ion radiotherapy (CIRT) is expected to be a promising treatment modality against hepatocellular carcinoma (HCC). In Japan, CIRT for hepatocellular carcinoma 4 cm or larger is now covered by public insurance, but the number of CIRT treatment centers is still small and further investigation of safety and efficacy is needed. The aim of this study is to evaluate the safety and efficacy of CIRT for HCC.
Methods: This is a single-center, retrospective cohort study. Patients underwent CIRT for HCC 4 cm or larger at our hospital from 2000 to 2022. The primary endpoint was overall survival (OS), and secondary endpoints were treatment-related adverse events, local control (LC), and progression-free survival (PFS).
Results: A total of 248 patients were include in this study. The median age was 74 years. The Child-Pugh classes A and B were 216 (87.1%) and 32 (12.9%), respectively. The BCLC staging A, B and C were 118 (47.6%), 38 (15.3%) and 92 (37.1%), respectively. Prescribed CIRT doses were (in relative biological effectiveness); 45-48 Gy in two fractions (n=133), 52.8-60 Gy in four fractions (n= 115). The median follow-up period was 30.6 months. The grade 3 adverse events according to CTCAE v5.0 were hepatobiliary disorders in 6 (2.4%) and dermatitis in 3 (1.2%). No adverse events of grade 4 or higher were observed. The OS, LC and PFS rates at 3 years were 66.7%, 86.9% and 25.8%, respectively.
Conclusion: CIRT for HCC 4cm or larger is an effective treatment with high safety and high local efficacy.

P-125
10081

Ablation Training Program for Liver Tumors at Juntendo

Shuichiro Shiina, Maki Tobari, Hitoshi Maruyama, Hiroaki Nagamatsu, Naoki Hotta, Terguunbileg Batsaikhan, Deng Qing, Lariza Marie L. Canseco, Javkhlan Maikhuu
Department of Gastroenterology, Juntendo University, Tokyo, Japan

Image-guided ablations, such as RFA and MWA, are potentially curative, minimally invasive, and easily repeatable for recurrence. However, ablations are highly operator-dependent, and the skills and outcomes can vary significantly from operator to operator. Juntendo is the highest-volume center for ablations and has the best 5-year survival rate for HCC in Japan. To disseminate skills and know-how for ablations, we have held 16 domestic training programs with 270 Japanese doctors participating and nine international programs with 121 foreign doctors attending. Programs included lectures, live demonstrations, and case studies. Lecture topics covered current status of ablations, ablation devices, ultrasonography, and more. During live demonstrations, RFA and MWA are performed on a wide variety of cases, including newly diagnosed cancers that are not difficult to ablate, tumors just below the diaphragm requiring artificial ascites, tumors in the caudate lobe, tumors adjacent to the heart, portal vein or hepatic vein, tumors over 5 cm, more than five tumors, and hepatic metastasis. We demonstrated the importance of appropriate patient posture, the usefulness of our original dedicated probe for interventional procedures and our ablation-dedicated operation table, and methods to perform ablations under Sonazoid guidance and with fusion imaging. In the case studies, difficult-to-ablate cases from participants' hospitals were presented and discussed. Many participants remarked on the benefit of being directly trained by noted interventional oncologists in an academic environment. The questionnaires revealed overwhelmingly positive feedback. Our programs may be useful in providing opportunities to understand basic concepts and learn essential technical tips for ablations.

P-126
10098

LI-RADS CT/MRI Radiation Treatment Response Assessment Version 2024: Evaluation after Transarterial Radioembolization for Hepatocellular Carcinoma

Sunyoung Lee
Department of Radiology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Background: This study aimed to compare the performance of the LI-RADS CT/MRI Radiation TRA version 2024 after transarterial radioembolization (TARE) for hepatocellular carcinoma (HCC) with that of the LI-RADS CT/MRI TRA version 2017.
Methods: This retrospective study included patients with HCC treated with TARE followed by hepatic surgery between November 2012 and April 2023 at two tertiary referral centers. Each treated lesion was assigned a LI-RADS treatment response (LR-TR) category using both the 2024 and 2017 TRA versions. The sensitivity and specificity of the two TRA algorithms in the consensus reading were compared using the McNemar test, with histopathology as a reference standard.
Results: A total of 46 (mean age, 56.2 years; 39 men) patients with 46 TARE-treated lesions (23 with histopathological incomplete necrosis) were included. The distribution of categories based on version 2024 was as follows: LR-TR Nonviable, 52.2%; LR-TR Nonprogressing, 39.1%; and LR-TR Viable, 8.7%. While no category change was noted for LR-TR Nonviable lesions between the two versions, 16 lesions classified as LR-TR Viable according to version 2017 were recategorized as LR-TR Nonprogressing according to version 2024. For predicting histopathological incomplete necrosis, the LR-TR Viable or Nonprogressing categories of version 2024 and the LR-TR Viable or Equivocal categories of version 2017 showed equivalent high sensitivity (87.0%; 95% confidence interval [CI]: 67.9-95.5) and specificity (91.3%; 95% CI: 73.2-97.6).
Conclusion: While applying the updated radiation TRA version 2024 resulted in recategorization, its diagnostic performance in predicting tumor viability was comparable to that of TRA version 2017.

P-128
10151

Clinical Outcomes with Stereotactic Body Radiation Therapy in Patients with Hepatocellular Carcinoma

Puja Sahai, Hanuman P Yadav, Ajit P Solanky, Vaishak Jawahar, Mangu S Bharadwaj, Jasim Jaleel, Guresh Kumar
Institute of Liver and Biliary Sciences, New Delhi, India

Background: The purpose of the present study was to evaluate outcomes with stereotactic body radiation therapy (SBRT) for patients with hepatocellular carcinoma (HCC).
Methods: The patients (n=23) had BCLC A, B or C disease with 1-3 new, residual, progressive, or recurrent lesions after prior liver directed treatments. Twenty-two patients had Child Pugh A (n=17) or B (n=5) cirrhosis. The dose fractionation for SBRT was 12-50 Gy in 3-10 fractions of 4-10 Gy each fraction. Six patients had received TACE and/or MWA after SBRT. Systemic treatment was given with SBRT in 19 patients. Treatment response was evaluated as per mRECIST and Kaplan-Meier survival analysis was performed.
Results: The median follow-up for surviving patients (n=4) 56.6 months (37.9-68.3). The median overall survival was 14.6 months (95% CI 6-23.2 months) and 30 months (95% CI 18.7-41.4 months) after SBRT and index cancer diagnosis, respectively. The 1-year, 2-year, and 3-year overall survival rates after diagnosis were 77.8%, 58.8%, and 44.1%, respectively (Fig 1). The 1-year and 2-year progression-free survival rates were 60% and 53.4% after SBRT. A decline in Child Pugh score of 2 or more points and 1 point was observed in 3 and 5 patients, respectively within 3 months after SBRT. ALBI grade at diagnosis (1 or 2 versus 3) was associated with survival (p=0.006), HR 5.95 (95% CI 1.65-21.5).
Conclusion: The present study showed disease control, survival benefit and tolerability with addition of SBRT with other modalities in HCC. A multidisciplinary approach incorporating SBRT is needed for long-term survival in HCC.

P-129
10071

Efficacy of the GFAD Index as a New Indicator for the Early Diagnosis of Non-Viral Hepatocellular Carcinoma

Akiyo Ishiguro[1], Mitsuaki Nishioka[2], Toshihiko Kobayashi[2], Yuki Kunimune[1,2], Yutaka Suehiro[1,2], Issei Saeki[3], Taro Takami[3], Takahiro Yamasaki[1,2]
[1]Department of Oncology and Laboratory Medicine, Yamaguchi University Graduate School of Medicine, Japan, [2]Division of Laboratory, Yamaguchi University Hospital, Japan, [3]Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Japan

Background: Previously, we reported that the GFAD index, which combines glycosylated ferritin (**G**-FER), total ferritin (**F**ER), **A**FP, and **D**CP, is useful for the early diagnosis of HCC. This study was designed to further evaluate the diagnostic performance of the GFAD index for HCC, especially early stage non-viral HCC.
Methods: We collected serum samples from 254 HCC patients: 133 with viral HCC and 121 with non-viral HCC. Among them, 26 patients were BCLC stage 0, and 60 patients were stage A. Serum samples were also collected from 195 non-cancer patients. After measuring AFP, DCP, G-FER, and FER, the GFAD index was calculated using a predictive formula based on a logistic regression model with variables including age, sex, and the above measures. We compared the diagnostic performance of GFAD with that of the AFP/DCP combination and the ASAP score, a highly accurate HCC diagnostic algorithm calculated from age, sex, AFP, and DCP.
Results: As the accompanying table shows, the GFAD index had a significantly higher AUC for discrimination between all HCC patients and non-cancer patients compared to that of the combination of AFP/DCP and the ASAP score. Similarly, the AUC of GFAD was also significantly higher than that of the AFP/DCP combination and the ASAP score in non-viral HCC. In early stage non-viral HCC, the GFAD index showed higher sensitivity and specificity than those of the AFP/DCP combination and the ASAP score.
Conclusions: GFAD was useful in detecting non-viral HCC even in the early stage with high sensitivity and specificity.

P-130
10087

The Association between the Prognoses and Systemic Chemotherapy According to the Oncological Conditions in Patients with Colorectal Liver Metastases

Nozomu Sakai, Tsukasa Takayashiki, Shigetsugu Takano, Daisuke Suzuki, Masayuki Ohtsuka
Department of General Surgery, Chiba University, Chiba, Japan

Background: Surgical resection is the gold standard treatment for colorectal liver metastases (CRLM). However, the prognosis is still poor in patients with aggressive tumor behavior, even after curative resection.
Patients and Methods: Medical records of 314 patients who underwent initial hepatectomy for CRLM between 2001 and 2022 were reviewed retrospectively.
Results: Patients were divided into three groups according to the Beppu score: low risk (score 0), intermediate risk (score 1-10), and high risk (score 11<). Overall survival (OS) and recurrence free survival (RFS) were clearly stratified according the score. Patients with neoadjuvant chemotherapy (NAC) had a significantly worse prognosis than that without NAC probably due to selection bias. To assess the effect of adjuvant chemotherapy (AC), NAC (+) patients were excluded. In the intermediate risk patients, OS was better in patients with AC (MST 140 vs. 46 months, p=0.05) and RFS was relatively better in patients with AC (MST 20 vs. 13 months, p=0.13). No beneficial effect of AC was found in patients with low and high risk.KRAS status was examined in 188 patients. In KRAS wild patients, RFS and OS were stratified into three groups. However, in KRAS mutant patients, there were no significant differences. In KRAS wild patients, OS was better in the AC (+) group (MST 74 vs 51 months, p=0.048).
Conclusion: The intermediate risk and KRAS wild-type patients may benefit from AC, while those with high risk and KRAS mutation have a poor prognosis and require multidisciplinary treatment with NAC and AC.

Poster Session

P-131
10095

Quality of Life in Patients with Hepatobiliary Cancers

Asmin Valiyagath
Al Iqbal Hospital, India

Purpose/Objectives: This study aims to describe the symptom concerns of patients with hepatocellular carcinoma (HCC) and pancreatic cancer and to examine how these symptoms impact their quality of life (QOL).
Methods: A descriptive, longitudinal study was conducted at a comprehensive cancer center, involving 39 patients undergoing treatment for either HCC or pancreatic cancer. Patients were tracked from the baseline for three months, with outcome measures assessed monthly. The Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) and the Functional Assessment of Chronic Illness Therapy-Spirituality Subscale (FACIT-Sp-12) were used to evaluate symptoms and QOL. Descriptive analyses were performed on demographic, treatment, and symptom data, followed by two-way repeated measures analysis of variance to compare FACT-Hep and FACIT-Sp-12 scores by diagnosis and treatment type.
Results: Patients with hepatobiliary cancers experience persistently poor quality of life, with this trend continuing over time. Commonly reported symptoms include abdominal pain, fatigue, weight loss, and poor appetite.
Conclusions: The findings highlight that patients with hepatobiliary cancers face multiple symptoms that adversely affect their overall quality of life. Domains such as physical and functional well-being are particularly concerning. Identifying and understanding these specific symptom and quality of life issues is crucial for improving clinical care and developing targeted multidisciplinary interventions for this underserved cancer population.

P-132
10097

Does Transcatheter Arterial Chemoembolization for Liver Metastasis in Neuroendocrine Tumors Reduce Hepatic Reserve?

Asako Nogami[1], Noritoshi Kobayashi[2], Naohiro Wada[1], Michihiro Iwaki[1], Takashi Kobayashi[1], Atsushi Nakajima[1], Masato Yoneda[1]
[1]Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, [2]Department of Oncology, Yokohama City University Graduate School of Medicine, Japan

Background: Repeated Transcatheter Arterial Chemoembolization (TACE) for hepatocellular carcinoma (HCC) is known to reduce liver function. However, there is limited data on the effects of TACE on liver function in patients with liver metastases of neuroendocrine tumors (NET). This study aimed to evaluate the impact of TACE on liver function in patients with NET liver metastases.
Method: Eight patients who underwent TACE for liver metastases of NETs between August 2014 and July 2024 at our hospital were included. Liver function was evaluated using the ALBI (Albumin-Bilirubin) score, a method for assessing liver function in patients with HCC. The ALBI score was calculated at three time points: before treatment, at the worst value during hospitalization, and one month after treatment.
Results: The study included 16 sessions with five male and three female patients. The mean age at the time of the procedure was 62.9 (50-74) years. Primary tumor sites included pancreatic (5 cases), rectal (1 case), small bowel (1 case), and unknown primary (1 case). All cases were classified as G2. Selective TACE was administered in five sessions. None of the cases were complicated by cirrhosis, and no ascites or hepatic encephalopathy occurred post-treatment. The ALBI score was -2.63/-1.76/-2.58 at the pre-treatment and post-treatment and after 1 month of treatment, indicating that liver function generally returned to pre-treatment levels.
Conclusions: TACE for NET liver metastases in patients without cirrhosis can be performed without compromising liver function. Given the small sample size, further longitudinal studies with larger cohorts are needed.

Poster Session

P-133
10101

Clinical Outcome of GCD Therapy for Unresectable Intrahepatic Cholangiocarcinoma

Hiroki Inada[1], Hiromitsu Hayashi[2], Yasuhito Tanaka[1]
[1]Department of Gastroenterology and Hepatology, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan., [2]Department of Gastroenterological Surgery, Graduate School of Life Sciences, Kumamoto University, Kumamoto, Japan

Background: Durvalumab/Gemcitabine/Cisplatin(GCD) therapy has become the first-line treatment for unresectable biliary tract cancer in Japan, but the results limited to intrahepatic cholangiocarcinoma(ICC) have not yet been reported.
Method: A retrospective analysis was performed on 41 ICC patients who were followed up with GC or GCD therapy at our hospital until January 2024.
Result: Survival analysis of 24 patients in the GC group and 17 patients in the GCD group, after Propensity Score Matching, showed a trend toward longer PFS in the GCD group (7.1 months vs. 10.6 months p=0.47). Next, prognostic factors for the GCD group were examined. The background of GCD group was as follows: Stage I/II/III/IV(0/1/0/16), distant metastasis: 11 (65%), primary treatment: 10 (59%), and CGP testing: 11 (65%). Best response was CR:0, PR:4, SD:10, PD:1, NE:2. 1 case reached conversion resection. In the multivariate analysis of factors contributing to OS, only the presence or absence of metastasis to other organs was extracted with significant differences. The OS without metastasis was significantly longer than those with metastasis (p=0.049). All patients who underwent CGP testing were found to have Druggable mutation. 4(24%) patients had a CDKN2A/B mutation, a known prognostic factor for BTC, but there was no significant difference in OS compared to the no-mutation group. 1 patient was started on a clinical trial based on the APC mutation.
Conclusion: The PD rate of GCD therapy is low and its potential as preoperative chemotherapy is promising, and sequential treatment with GCD therapy and genomic medicine is expected.

P-134
10105

Etiological Transitions in Patients with Liver Cirrhosis and Hepatocellular Carcinoma: A Single-center Study from an Institution Located in a District with a High Prevalence of Viral Hepatitis

Hirayuki Enomoto, Tomoyuki Takashima, Nobuhiro Aizawa, Naoto Ikeda, Yukihisa Yuri, Taro Kimura, Kohei Yoshihara, Ryota Yoshioka, Shoki Kawata, Yuta Kawase, Ryota Nakano, Hideyuki Shiomi, Takashi Nishimura, Shinya Fukunishi, Hiroko Iijima, Shinichiro Shinzaki
Department of Gastroenterology, Hyogo Medical University, Hyogo, Japan

Background: A recent nationwide survey has shown that the contribution of viral hepatitis as an etiology of liver cirrhosis (LC) is suggested to have been decreasing in Japan (Hepatol Res. 2024, in press). Our institution is located in a district with a markedly high prevalence of viral hepatitis. We investigated the details of inpatients, focusing on the contribution of viral hepatitis-related cirrhosis and hepatocellular carcinoma (HCC).
Methods: We classified inpatients of our department into four groups (diagnosed in -2007, 2008-2012, 2013-2017, and 2018-2021) and analyzed the changing trends in the etiologies of LC (N=1568) and HCC (N=980).
Results: Regarding the etiologies of LC, the contribution of viral hepatitis-related cirrhosis decreased from 81.1% to 58.9%. In particular, hepatitis virus C (HCV)-related cirrhosis was found to have dropped from 70.2% to 43.0%. In contrast, the ratios of alcohol-associated liver disease (ALD)-related LC and NASH-related LC increased (from 9.9% to 18.0% and from 0.3% to 10.8%, respectively). Regarding the etiologies of HCC, the contribution of viral hepatitis-related HCC remarkably decreased from 91.8% to 74.9%. HCV-related HCC was found to have also declined from 82.6% to 54.7%. The ratios of ALD-related LC and NASH-related LC increased (from 3.6% to 11.7% and from 0.0% to 10.1%, respectively).
Conclusions: Our data in daily practice from an institution located in a district with a high prevalence of viral hepatitis was consistent with the recent nationwide survey regarding the etiologies in LC and HCC, depicting a decreasing trend in viral hepatitis and increasing trend in non-viral liver diseases.

P-135 10140 Atezolizumab plus Bevacizumab for Combined Hepatocellular Cholangiocarcinoma

Tomoyuki Satake, Mitsuhito Sasaki, Hiroshi Imaoka, Taro Shibuki, Kazuo Watanabe, Kanae Inoue, Tomonao Taira, Shota Yamaguchi, Go Igarashi, Shuichi Mitsunaga, Masafumi Ikeda
Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Combined hepatocellular cholangiocarcinoma (cHCC-CCA) is a rare subtype of primary liver cancers. Therapeutic strategies for patients with cHCC-CCA are limited, and no standard systemic treatment has been established for unresectable cHCC-CCA. We have treated six patients of cHCC-CCA with atezolizumab plus bevacizumab. Of the six patients, five patients were male, five patients were Child-Pugh class A, two patients had HCV, and four patients were Barcelona Clinic Liver Cancer (BCLC) stage C. Atezolizumab plus bevacizumab was administered in four patients for first-line treatment and two patients for second-line treatment. Three patients achieved a partial response and one achieved a stable disease as the best responses, whereas the two patients were unable to continue treatment owing to adverse events. Atezolizumab plus bevacizumab should be an effective treatment for unresectable cHCC-CCA.Our group, JON-HBP (Japan Oncology Network in Hepatobiliary and Pancreas), has a platform, the MASCARPONE study, for the development of treatments for rare subtypes of hepatobiliary and pancreatic cancer. Based on our above results, we have now launched an open-label, multicenter, investigator-initiated phase II clinical trial to evaluate the efficacy and safety of atezolizumab plus bevacizumab in patients with advanced cHCC-CCA.

P-136 10070 A Novel Hepatitis Delta Virus (HDV) in Vitro Carcinogenesis Model

Shinya Sato, Kosuke Kaji, Tadashi Namisaki, Hitoshi Yoshiji
The Department of Gastroenterology, Nara Medical University, Nara, Japan

Background: We established a robust and reproducible model to study the carcinogenesis by hepatitis delta virus (HDV) based on HDV transfection in the absence of hepatitis B virus.
Methods: Huh7 hepatoma cell line was transfected with a plasmid vector pSVL(D3), which harbors a trimer of the HDV genome, for 3, 6, 9, and 12 days to collect cell lysate, supernatant, RNA and fix cells for immunofluorescence (IF). The carcinogenic effect of HDV was assessed with real time PCR and in situ hybridization (FISH) of HDV-RNA, IF and Western blot (WB) of hepatitis delta antigens (HDAgs), and RNA-Seq.
Result: HDV-RNA increased after 24h of transfection and plateaued around day 6, in consistent with intrahepatic HDAg (WB). IF showed that only the small HDAg are expressed at day 3, while large HDAg-positive cells started to appear at day 6. The positivity of both antigens continued to increase to the parity at day 9 and 12. HDV-RNA was detectable in the nucleus at 3 and 6 days post-transfection and then in the cytoplasm from 9 days onward (FISH). Moreover, RNA-Seq and gene ontology analysis revealed that expression of genes involved in cell cycle, DNA damage, and DNA repair are unregulated.
Conclusion: Our in vitro model recapitulated HDV replication and induction of the genome instability by HDV and thus may be useful to study the viral carcinogenesis.

P-137
10091

The Prognosis of Hemodialyzed Patients with Hepatitis C Treated by Direct Acting Antivirals

Hitoshi Takagi, Satoshi Takakusagi, Takashi Kosone, Toshiharu Noguchi
The Department of Internal medicine, Kusunoki Hospital, Fujioka Gunma Japan

Background: Hemodialysis (HD) patients of chronic renal failure (RF) complicated with chronic hepatitis or liver cirrhosis C (HD-CH) have been successfully and safely treated by direct acting antivirals (DAA), however the prognosis after SVR may not be simply good enough due to their diverse comorbidities.
Patients and Method: Twenty HD-CH were treated by DAA from 2014 to 2021in Kusunoki Hospital and overall prognosis was investigated until July 2024. Two females and 18 males were included. Age ranged from 49 to 81, median 71 years old. At the beginning of DAA for CH, the duration of HD ranged from 2 months to 32 years, median 8 years.
Results: All the 20 patients gained SVR by DAA. Eleven patients died after the achievement of SVR from 4 months to 8.5 years, median 5 years. The other 9 cases survived from 3 to 10 years, mean 6.8 years, median 6 years. The causes of death were as follows; 3 cases of cerebral hemorrhage, 3 of pneumonia, each one of acute myeloblastic leukemia, renal cell carcinoma, hepatic failure of unknown origin (hepatocellular carcinoma, possible), sudden death of unknown origin, operation death for aortic valve stenosis.
Conclusion: DAA could eliminate HCV in HD-CH and resulted the decrease of liver related death, however more than half of them died of non-liver related complications within median 5 years compared with 6.8 years of survivor. Total health care might be more important than SVR in HD-CH.

P-138
10094

Comprehensive RNA-seq Analysis of HCV-infected Cells and Specimens from Patients with Liver Cancer after HCV Eradication to Elucidate Liver Carcinogenesis

Katsuya Nagaoka[1], Toru Okamoto[2], Takashi Matsumoto[3], Tomonori Tsuyama[4], Hiromitsu Hayashi[3], Takehisa Watanabe[1], Hiroko Setoyama[1], Yasuhito Tanaka[1]
[1]Gastroenterology and Hepatology, Kumamoto University, Japan, [2]Microbiology, Juntendo University School of Medicine, Japan, [3]Gastroenterological Surgery, Kumamoto University, Japan, [4]Center for Metabolic Regulation of Healthy Aging, Kumamoto University, Japan

Background and Aim: The molecular mechanisms of liver carcinogenesis in patients with sustained virologic response (SVR) after persistent hepatitis C virus (HCV) infection remain unclear. The aim of this study was to elucidate the underlying changes in gene expression profiles.
Methods: Two experiments were performed in liver-derived Huh7 cells: (1) overexpression of GFP alone, HCV core protein-GFP, and Japanese encephalitis virus-GFP for comparison; (2) HCV infection and clearance, with cells prepared (i) 4 days post-infection, (ii) 7 days after daclatasvir treatment, and (iii) 10 days after drug-free culture. In addition, samples were prepared from cancerous and adjacent non-cancerous tissues (N=6) from surgically resected patients with post-SVR hepatocellular carcinoma (HCC). RNA-seq analysis and bioinformatic analyses were performed on these samples.
Results: The gene sets "cholesterol synthesis disorders" and "retinoblastoma gene in cancer" were identified as specifically downregulated by HCV core protein overexpression and upregulated after HCV clearance in vitro experiments. Other gene sets such as "G1 to S cell cycle control" were also upregulated after HCV clearance. Furthermore, in the HCC tissues of surgically resected specimens, the "retinoblastoma gene in cancer" remained upregulated, and a significant upregulation of the "G1 to S cell cycle control" gene set was observed.
Conclusion: The results suggest that the expression changes in the "retinoblastoma gene in cancer" gene set induced by the HCV core protein may partially affect the early stage of the multistep process leading to carcinogenesis after HCV infection and SVR.

Poster Session

P-139
10096

Epidemiology of Liver Disease in Kerala: A Retrospective Study

Sabin Katpattil
Mother Hospital, India

Introduction: India, with its diverse population, exhibits varying patterns of liver disease across different regions. This study aims to analyze and describe the distribution and patterns of liver diseases in Kerala, a state in South India.
Materials and Methods: This retrospective study reviewed patient data from the seven administrative divisions of Kerala, covering the period from January 2021 to 2023. The data included cases of liver diseases managed at hepatology departments across the state.
Results: The study encompassed 3,225 patients, aged 15 to 80 years, with a predominance of males (67.9%). Among all patients presenting to hepatology departments, 13.2% were diagnosed with liver diseases. The majority of these patients (77.35%) were actually suffering from nonulcer dyspepsia or irritable bowel syndrome rather than liver diseases. Chronic liver diseases (CLDs) were the most common diagnosis, affecting 37% to 69% of patients. Complications such as hepatic encephalopathy were less frequently observed in regions with a more advanced healthcare system. Nonviral infections, including liver abscesses and biliary ascariasis, were also present. Acute hepatitis emerged as a significant concern, accounting for approximately 20% of cases.
Conclusion: This study reveals a diverse distribution of liver disease patterns across Kerala, reflecting regional variations in healthcare access and disease prevalence. Understanding these regional disparities is crucial for improving diagnosis, treatment, and management strategies for liver diseases in the state.

P-140
10021

Oncolytic Activity of a Chimeric Influenza A Virus Carrying a Human CTLA4 Antibody in Hepatocellular Carcinoma

Penghui Yang, Hao Yang, Yan Xu, Cong Li, Fei Wang, Zhaohai Wang, Minggen Hu, Xuan Zhang, Rong Liu
First Medical Center, Chinese PLA General Hospital, Beijing, China

Introduction: Oncolytic virotherapy belongs to a kind of active immunotherapy, which could trigger a potent antitumor immune response, showing great potential in clinical application. OVs could induce immune responses through the dual mechanisms of selective tumor killing without destroying normal tissues and induction of systemic antitumor immunity.
Methods: In this study, we successfully rescued a chimeric oncolytic influenza virus carrying a human CTLA4 antibody in the background of the A/PR/8/34 (PR8) virus. The chimeric virus, called rFlu-huCTLA4, contained the heavy and light chains of the human CTLA4 antibody in the PB1 and PA segments of the PR8 virus, respectively.
Results: The first-generation hemagglutination (HA) titers of the rFlu-huCTLA4 virus ranged from 27 to 28. The rFlu-huCTLA4 virus could effectively replicate in various cells in time- and dose-dependent manners. ELISA assay revealed that the secreted huCTLA4 antibody levels in chicken embryos increased gradually over time. Furthermore, MTS and crystal violet analysis showed that the selective cytotoxicity of the virus was higher in hepatocellular carcinoma cells than in normal liver cells. In vivo experiments displayed that rFlu-huCTLA4 reduced tumor growth and increased the survival of mice compared with the PR8 group. More importantly, in the rFlu-huCTLA4 group, we found that CD4+ and CD8 +T cells were significantly increased in tumor-bearing BALB/c mice.
Conclusion: Taken together, these findings demonstrated that the chimeric oncolytic virus rFlu-huCTLA4 could selectively destroy hepatocellular carcinoma cells in vitro and in vivo and may provide a promising clinical strategy for targeted immunotherapy of HCC with the oncolytic flu virus.

P-141
10024

Cabozantinib Prevents the Progression of Metabolic Dysfunction-associated Steatohepatitis by Inhibiting the Activation of Hepatic Stellate Cell and Macrophage and Attenuating Angiogenic Activity

Takuya Matsuda, Kosuke Kaji, Norihisa Nishimura, Shohei Asada, Aritoshi Koizumi, Misako Tanaka, Nobuyuki Yorioka, Yuki Tsuji, Koh Kitagawa, Shinya Sato, Tadashi Namisaki, Takemi Akahane, Hitoshi Yoshiji
The Third Department of Internal Medicine, Nara Medical University, Nara, Japan

Background: Cabozantinib, a multiple tyrosine kinase inhibitor targeting AXL, VEGFR, and MET, is used clinically to treat certain cancers, including hepatocellular carcinoma. This study aimed to assess the impact of cabozantinib on liver fibrosis and hepatocarcinogenesis in a rat model of metabolic dysfunction-associated steatohepatitis (MASH).
Methods: MASH-based liver fibrosis and hepatocarcinogenesis were induced in rats by feeding them a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) for eight and 16 weeks, respectively. Cabozantinib was administered concurrently with the diet in the fibrosis model and after eight weeks in the carcinogenesis model.
Results: Treatment with cabozantinib significantly attenuated hepatic inflammation and fibrosis without affecting hepatocyte steatosis and ballooning in CDAHFD-fed rats. Cabozantinib-treated rats exhibited a marked reduction in α-smooth muscle actin-positive activated hepatic stellate cell (HSC) expansion, CD68+ macrophage infiltration, and CD34+ pathological angiogenesis, along with reduced hepatic AXL, VEGF, and VEGFR2 expression. Consistently, cabozantinib downregulated the hepatic expression of profibrogenic markers, inflammatory cytokines, and proangiogenic markers. In a cell-based assay of human activated HSCs, cabozantinib inhibited Akt activation induced by GAS6, a ligand of AXL, leading to reduced cell proliferation and profibrogenic activity. Meanwhile, administration of cabozantinib did not affect Ki67+ hepatocyte proliferation or serum albumin levels, indicating no negative impact on regenerative capacity. Treatment with cabozantinib also reduced the size and number of placental glutathione transferase-positive preneoplastic lesions in CDAHFD-fed rats.
Conclusion: cabozantinib shows promise as a novel option for preventing MASH progression.

P-142
10028

Extracellular Vesicles-mediated Mutant β-catenin Transfer from Hepatocyte Activates Hepatic Stellate Cells in Tumor Microenvironment

Yu Ota[1,2], Irene K Yan[2], Julia Driscoll[2], Shin Otake[1], Hidemi Hayashi[1], Takumu Hasebe[1], Shunsuke Nakajima[1], Koji Sawada[1], Kazunobu Aso[1], Mikihiro Fujiya[1], Tushar Patel[2]
[1]Division of Gastroenterology, Department of Internal Medicine, Asahikawa Medical University, Hokkaido, Japan, [2]Department of Cancer Biology, Mayo Clinic, Jacksonville, FL, USA

Background: The aberrant activation of Wnt/β-catenin signaling is implicated in hepatocellular carcinoma (HCC) progression and hepatic stellate cells (HSC) activation. Although the crosstalk between HCC and activated HSC has been reported, the molecular mechanisms of this crosstalk are unknown. It is known that extracellular vesicles (EVs) can transfer mutant β-catenin to the recipient cells, but it remains unclear whether the transfer of β-catenin via EVs can activate HSC. Therefore, we focused on the association of mutant β-catenin with EVs in HSC activation.
Methods: Non-malignant human hepatocytes (HH) and human HSC (LX-2) were used and EVs were isolated by the Tangential Flow Filtration System. HCC mouse model was generated by co-expression of cMET and mutant β-catenin using a sleeping beauty transposon/transposase system. The activation of Wnt/β-catenin signaling were confirmed by TOP/FOP Flash luciferase reporter assay.
Results: The expression of β-catenin or α-SMA and the ratio of TOP/FOP were increased in LX-2 transduced with mutant β-catenin vector. We confirmed that mutant β-catenin was contained in EVs from HH transduced with mutant β-catenin vector. The expression of β-catenin or α-SMA and the ratio of TOP/FOP in LX-2 incubated with these HH-derived EVs. Nuclear and cytoplasm staining of β-catenin could be appreciated in HCC mouse model and α-SMA staining could be detected within HCC stroma.
Conclusions: Mutant β-catenin activated HSC via hepatocyte-derived EVs *in vitro*, and induced hepatocarcinogenesis in the presence of c-MET and promoted activation of HSC *in vivo*. Our findings provide new insights into HSC activation via EVs in tumor microenvironment.

P-143
10032

Tumor-derived CCL15 Regulates RNA m6A Methylation in Cancer-associated Fibroblasts to Promote Hepatocellular Carcinoma Growth

Yueguo Li
Tianjin Medical University Cancer Hospital and Institute, China

Background and Aims: HCC is a lethal malignancy characterized by rapid growth. The interaction between tumor cells and cancer-associated fibroblasts (CAFs) significantly influences HCC progression. CCL15 is predominantly expressed in HCC and strongly correlates with tumor size, indicating its critical role in HCC growth. However, previous studies suggest that CCL15 doesn't directly stimulate cancer cell proliferation. The specific role and mechanism of CCL15 in HCC proliferation remain unknown.
Approach and Results: Through single-cell RNA sequencing data and immunofluorescence, we identified that CCL15 was predominantly overexpressed by HCC cells. Furthermore, we discovered that CCL15 promotes HCC growth by stimulating the crosstalk between HCC cells and CAFs via CCR1 signaling, as evidenced by co-culture assays, organoid models, and allograft models. Mechanistically, CCL15 induced the expression of FTO in CAFs through the STAT3 pathway. By m6A sequencing and RNA sequencing, we found that CEBPA mRNA, a transcription factor regulating CXCL5 expression, was a target of FTO. CXCL5, secreted by CAFs, activated the CXCR2 receptor on HCC cells and enhanced their proliferation. Notably, we found that interfering with CCL15 signaling using a neutralizing antibody attenuated HCC growth in heterotypic co-injection and patient-derived xenograft murine models. Finally, CXCL5 also upregulated CCL15 expression in HCC cells by modulating P53 expression through MDM2, forming a positive feedback loop.
Conclusions: Our study unveiled CCL15 as a key mediator in HCC progression, facilitating communication between HCC cells and CAFs. This highlighted a novel regulatory axis in HCC and suggested that targeting CCL15 could be a potential therapeutic strategy.

P-144
10112

A Near-infrared-modulated System Enabling Efficient Delivery of Glucose Derivative as a New Therapeutic Strategy for Liver Cancer

Sohji Nishina[1], Kyo Sasaki[1], Keisuke Hino[2]
[1]Department of Gastroenterology and Hepatology, Kawasaki Medical School, Kurashiki, Japan, [2]Digestive Disease Center, Shunan Memorial Hospital, Kudamatsu, Japan

Background: 2-Deoxy-D-glucose (2DG), a glucose derivative, has been reported to have cytotoxic effects against several cancers. However, the clinical application of 2DG was not recognized because of adverse events due to high dose administration. We developed cancer-specific drug delivery system (DDS) using 2DG encapsulated poly [lactic-co-glycolic acid (PLGA) nanoparticles(CMGH 2021). This system showed strong antitumor effect by cytotoxicity and antitumor immunity without any adverse events in mouse HCC models. The aim of this study was to assess antitumor effect of a novel DDS which delivers and releases 2DG more efficiently into cancer cells, using thermodynamic cell engineering.
Methods: We engineered the liposomal nanoparticles (LNPs) where 2DG was encapsulated and a photothermal agent (a near-infrared absorbing dye) was embedded in the lipid membrane. The surface of LPNs was modified with cancer cell-targeting cyclic peptide (iRGD). Consequently, this engineered LNPs (termed as iRGD-2DG-nanoheater [iRGD-2DG-NanoHT]) was more specifically delivered to tumor cells and enabled more vigorous release of 2DG through the phase transitions after near-infrared irradiation.
Results: We found that iRGD-2DG-NanoHT was much more accumulated in liver tumors than 2DG-NanoHT in DEN-treated mice. Compared with 2DG alone, iRGD-2DG-NanoHT exhibited more vigorous antitumor effect, which promoted ferroptosis evidenced by GPx4 downregulation and increased the release of high mobility group box-1 (HMGB-1) that functions as damage-associated molecular pattern (DAMP). Interestingly, iRGD-2DG-NanoHT also enhanced antitumor immunity demonstrated by increased CD8+Tcell infiltration and suppressed Treg infiltration.
Conclusion: iRGD-2DG-NanoHT which exhibits more cytotoxicity and antitumor immunity may be a promising DDS as a new therapeutic strategy for HCC.

P-145
10164

Chemoprotective Effect of Crocetin-Dextrin Nano-formulation against N-Diethylnitrosamine Induced Hepatocellular Carcinoma in Rats via Mitochondrial Apoptosis and PI3K/Akt/mTOR Signaling Pathways

Vikas Kumar[1], Firoz Anwar[2]
[1]Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, Prayagraj, India, [2]King Abdulaziz University, Jeddah, Saudi Arab

Hepatocellular carcinoma (HCC) is known to have a high prevalence, particularly in regions with a high incidence of chronic liver diseases such as hepatitis B and C infections, alcoholic liver disease, and non-alcoholic fatty liver disease. In this study, we fabricate the crocetin-dextrin nano-formulation (CDNF) against N-diethylnitrosamine (DEN) induced hepatic cancer in rats. Crocetin-Dextrin nano-formulation was prepared the aqueous nano-emulsion of crocetin and dextrin. The Wistar rats divided into different groups and DEN (200 mg/kg) were for the induction of HCC in rats. The microscopical study was carried out for the confirmation of hepatic nodules. Hepatic, non-hepatic, antioxidant, cytokines and inflammatory parameters were estimated. The level of AKT, mTOR, Bax, p-53, Bcl-2, caspase-3 and PI3K gene were estimated. CDNF treatment remarkably reduced the tumor size, average size of nodules and tumor nodules. CDNF suppressed the level of AFP, AST, ALT, ALP, albumin, bilirubin, total protein and CRP level. CDNF also altered the level of antioxidant parameters like MDA, GPx, GSH, CAT and NO level. CDNF significantly reduced the level of TNF-alpha, IL-1beta, IL-6 and improved the level of IL-10. CDNF also suppressed the level of inflammatory parameters viz., COX-2, PGE2, VEGF and iNOS, respectively. CDNF also altered the level of gene expression like AKT, mTOR, Bax, p-53, Bcl-2, caspase-3 and PI3K. Histopathological observation suggest that CDNF treated rats exhibited the less necrosis, inflammatory cells. The result suggests that CDNF was able to alter the HCC in the rats via regulation of Bax/Bcl-2/p53 and PI3K/Akt/mTOR signaling pathways.

P-146
10168

The Whole Genome and RNA Sequence Analysis on the Hepatocellular Carcinoma Derived from the Patients with Fontan-associated Liver Disease

Taiji Yamazoe, Eiji Kakazu, Michitaka Matsuda, Taizo Mori, Sachiyo Yoshio, Tatsuya Kanto
Department of Liver Diseases, National Center for Global Health and Medicine, Chiba, Japan

Fontan-associated liver disease (FALD) is characterized by a congestive hepatopathy and develops liver cirrhosis and hepatocellular carcinoma (HCC) after 15-20 years of the Fontan procedure. To understand FALD hepatocarcinogenesis, we performed the analysis of the whole genome sequences (WGS) and RNA sequences (RNAseq).
We sequenced 8 paired tumors and non-tumors including focal nodular hyperplasia of the surgically resected specimens with NovaSeq6000, and used Mutect2 and GRIDSS-GRIPSS pipeline for variant call.
We observed FALD tumor has higher tumor mutational burden (TMB) than the TCGA liver cancer cohort, LIHC. The median TMB of the FALD HCCs were 4.6 (range 3.72-5.82) mutations / Mb. There was no mutation of TERT promoter, TP53, CTNNB1 or ARID1A, but mutations of RPS6KA3, RB1 and AXIN1. Compared with the ICGC liver cancer cohort, LIRI whose SV data is publicly available, the short (< 1 Mb) deletion and the translocation were significantly higher in FALD HCC. The SV call revealed that the deletion and disruption of TP53 and the homozygous deletion of RB1. The Hoshida's molecular subclass of FALD HCCs based on RNAseq were S1 and S2, which are "proliferation class". Based on the immune profiles inferred by the immune cell deconvolution, CIBERSORT, we classified HCCs into 6 class of immune subtypes. Our samples mainly belonged to two classes characterized by PD-L1 high or M0 macrophages.
We performed WGS and RNAseq of 8 paired samples derived from HCC patients with FALD. The findings suggested that FALD HCC specific phenotype, which is different from the HCC with other etiologies.

P-147
10009

Development of a Small Animal Model for Fatty Liver-related Hepatocarcinogenesis Research

Daiki Miki, Yusuke Tanaka, Masataka Tsuge, Yasutoshi Fujii, Shinsuke Uchikawa, Hatsue Fujino, Atsushi Ono, Eisuke Murakami, Tomokazu Kawaoka, Shiro Oka
Department of Gastroenterology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

Background: Recently, fatty liver-associated hepatocellular carcinoma has been on the rise worldwide. However, the molecular mechanism is not fully understood. As one means of clarifying this, we attempted to construct a small animal model of fatty liver.
Methods: Human hepatocyte chimeric mice were recognized as very useful for hepatitis virus research. On the other hand, it was reported that the chimeric mouse liver was spontaneously became fatty in the human(h)-hepatocyte regions. Infusion of h-growth hormone (GH) drastically decreased steatosis, showing the direct cause of h-GH deficiency in the generation of hepatic steatosis. In this study, we generated mice with varying degrees of fatty liver by combining a high-fat diet with GH supplementation and performed metabolomics analysis using their hepatocytes.
Results: As a result of collating the output data of CE-MS and LC-MS with the standard metabolite database of about 1300, a total of 437 metabolites were detected. Twelve triacylglycerol metabolites were detected and all of them tended to be higher in the high-fat diet group than in the reference group. As for fatty acids, sixteen metabolites were detected and all of them tended to be higher in the high-fat diet group. Sirius Red staining revealed fibrosis radiating from the venule and surrounding individual hepatocytes.
Conclusions: We developed a small animal model of fatty liver with fibrosis. It is expected to be useful for elucidating the molecular mechanism of fatty liver-related hepatocarcinogenesis in the future.

P-148
10039

Withdrawn

P-149
10047

Inhibitory Effects of Putrescine on Metabolic Dysfunction-associated Steatohepatitis in Mice

Erdenetsogt Dungubat[1], Yuko Yamada[1], Shinichiro Ohno[1], Tomohiro Umezu[1], Bin Shen[1], Akira Saitoh[1], Hajime Horiuchi[1], Masahiko Kuroda[1], Hirosuke Tawara[2], Mitsuko Sutoh[2], Naoki Ohkura[3], Hiroki Takahashi[4], Naoki Harada[4], Ryoichi Yamaji[4], Hiroyuki Kusano[5], Emiko Udo[6], Bungo Furusato[6], Toshio Fukusato[7], Yoshihisa Takahashi[1]

[1]Department of Molecular Pathology, Tokyo Medical University, [2]Institute for Animal Reproduction, [3]Laboratory of Host Defence, School of Pharma-Sciences, Teikyo University, [4]Department of Applied Biological Chemistry, Graduate School of Agriculture, Osaka Metropolitan University, [5]Department of Pathology, School of Medicine, International University of Health and Welfare, [6]Clinical Genomics Center, Nagasaki University Hospital, [7]General Medical Education and Research Center, Teikyo University, Japan

Background: Putrescine is a representative polyamine. Although several studies have shown inhibitory effects of other polyamines on metabolic dysfunction-associated steatohepatitis (MASH), no studies have examined effects of putrescine on MASH. In the present study, we examined effects of putrescine on model mice of MASH.
Methods: Eight-week-old male db/db mice were divided into the following groups: control diet and tap water (control), choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) and tap water (CDAHFD), CDAHFD and tap water supplemented with 0.4 g/L putrescine (putrescine). After 6 weeks, the mice were sacrificed and serum biochemical, histopathological, and molecular analyses were performed.
Results: Serum alanine aminotransferase (ALT) levels were significantly higher in the CDAHFD group than in the control group and significantly lower in the putrescine group than in the CDAHFD group. On image analysis, fibrosis was significantly more severe in the CDAHFD group than in the control group and significantly milder in the putrescine group than in the CDAHFD group. The number of myeloperoxidase-positive cells was significantly larger in the CDAHFD group than in the control group and significantly smaller in the putrescine group than in the CDAHFD group. Hepatic expression levels of peroxisome proliferator-activated receptor (PPAR)-α and PPAR-γ tended to be lower in the CDAHFD group than in the control group and tended to be higher in the putrescine group than in the CDAHFD group.
Conclusion: Putrescine inhibited markers of inflammation, liver cell injury, and fibrosis in MASH in mice. The effects might be associated with hepatic expression levels of PPAR-α and PPAR-γ.

P-150
10119

Exploring the Link Between Mitochondrial ROS, Peroxiredoxin V, and Liver Fibrosis in Metabolic Associated Fatty Liver Disease

Hyun Ae Woo[1], Ho Jin Yi[2], Ji Young Park[1]

[1]College of Pharmacy, Graduate School of Pharmaceutical Sciences, Ewha Women's University, Seoul, Republic of Korea, [2]Graduate School of Applied Science and Technology for Skin Health and Aesthetics, Ewha Women's University, Seoul, Republic of Korea

Metabolic Associated Fatty Liver Disease (MAFLD) encompasses a spectrum of liver conditions, including cirrhosis, hepatocellular carcinoma, and non-alcoholic steatohepatitis, originating from simple steatosis. Under normal conditions, fatty acid oxidation occurs predominantly in mitochondria, generating energy. However, in MAFLD, the excessive influx of fatty acids saturates mitochondrial β-oxidation, shifting the oxidation process to peroxisomes and microsomes, which increases reactive oxygen species (ROS) production. Consequently, hepatic mitochondria play a crucial role in the pathogenesis of MAFLD. We investigated the effects of mitochondrial ROS on MAFLD progression. Peroxiredoxin V (Prx V), a type of peroxidase, reduces peroxides such as hydrogen peroxide via reactive cysteine residues at active sites, and is significant in mitochondrial redox signaling. Our study confirmed that Prx V provides protection against liver damage induced by a methionine-choline-deficient (MCD) diet. Prx V knockout (KO) mice exhibited more severe liver damage compared to Prx V wild-type (WT) mice under the same conditions. These findings demonstrate the protective role of Prx V in mitigating liver damage and potentially liver fibrosis in MAFLD.

P-151
10167

Efalizumab Modulates HAT1 and Increases IL-9 to Induce Ferroptosis and CD8+ T Cell Immunological Activity in Hepatocellular Carcinoma

Manvendra Singh[1], Deepika Singh[2]
[1]Handia Hmfa Miet, India, [2]Shuats Sihas

Background: Pharmacological intervention targeting ferroptosis, a new form of controlled cell death function outside of the apoptotic mechanism, can boost cell immunological activity of anti-PD1 immunotherapy in hepatic cancer. In this work, we examined how Efalizumab affected ferroptosis and immunological activity in hepatocellular carcinoma.
Method: First, we performed RNA-sequencing in Efalizumab -treated HepG2 cells and found that Efalizumab significantly altered the expression of VEGF, PI3K, HAT1, SLC7A11, and IL-9 in hepatocellular carcinoma, upregulated 37 ferroptosis-related drivers, and downregulated 17 suppressors.
Result: It was observed that Efalizumab drove VEGF/PI3K/HAT1/SLC7A11 axis to induce hepatocellular carcinoma cell ferroptosis. Clinical evidence showed that VEGF expression was favorably correlated with PI3K, HAT1, and SLC7A11 in hepatic tissues. We found that Efalizumab increased tumor immune-microenvironment immune cell activation. In hepatocellular carcinoma cells, HAT1 up-regulated miR-143 targeting IL-9 mRNA 3'UTR. Efalizumab treatment increased IL-9 levels and secretion via the VEGF/PI3K/HAT1/miR-143/IL-9 axis, which inhibited tumor growth in vivo by increasing IL-2 and Granzyme B release from activated CD8+ T cells. In liver cancer, Efalizumab inhibits angiogenesis, causes ferroptosis, and boosts CD8+ T cell immunological activity.
Conclusion: This study illuminates how Efalizumab synergistically controls ferroptosis and CD8+ T cell immunological activity in hepatocellular carcinoma.

P-152
10170

Invasive Hepatic Stellate Cell Shapes Immunovascular Landscape of Hepatocellular Carcinoma

Michitaka Matsuda, Shinji Kondo, Tatsuya Kanto
National Center for Global Health and Medicine, Japan

Background: Hepatic stellate cells (HSC) are known as fibrogenic cells in the liver. Recently, we and other groups reported that HSC-derived heterogeneous CAF populations promote liver cancer. The study aims to elucidate how HSC acquires diverse CAF phenotypes and impacts the tumor microenvironment (TME).
Methods: GeoMx Spatial transcriptome (spRNA-seq) was conducted on Hepatocellular carcinoma (HCC) specimens resected from cirrhotic patients, where fibrosis area was defined by using collagen staining and fibrosis area-specific transcriptomes were obtained. Single-cell RNA sequence (scRNA-seq) was conducted on the frozen liver blocks from the matched patient. With Collagen hydrogel invasion assay, HSC at the differential invasion state was collected for RNA-seq.
Results: Integrative analysis of spRNA-seq and scRNA-seq resolved the cellular landscape of the fibrotic liver with HCC. While the fibrosis area consists of heterogeneous endothelial, immune, and mesenchymal populations, their composition and phenotype differ by location. Peritumor fibrosis contains more artery-like endothelial cells and less active immune populations than background fibrosis. HSCs at peritumor were angiogenic and immunosuppressive, suggesting HSCs regulate immune/vascular phenotype in the TME. Invasion assay elucidated phenotypic change of HSCs during the invasion, angiogenic at the early and immunosuppressive at the late phase. The invasion-associated genes of HSC were enriched at peritumor, suggesting HSC invasion occurs at peritumor and generates heterogeneous CAF populations.
Conclusion: By integrating the transcriptomics from three different assays, scRNA-seq, spRNA-seq, and collagen hydrogel invasion assay, we elucidated previously unrecognized phenotype of HSC during TME formation. Invasive HSC interacts with a vascular and immune system to generate unique TME around HCC.

Poster Session

P-159
10171

Investigation of TEAD Inhibitor for Hepatocellular Carcinoma Treatment

Yoshinobu Saito[1,2], Hayato Hikita[1], Takahiro Kodama[1], Robert Schwabe[2], Tetsuo Takehara[1]
[1]Osaka University Graduate School of Medicine Gastroenterology and Hepatology, [2]Columbia University Department of Medicine, Japan

Background/Aim: Recent advancements in cancer drug therapy (CDT) have expanded treatment options for advanced hepatocellular carcinoma (HCC), including multi-kinase inhibitors and combination immunotherapy. However, no cancer cell-specific drugs are currently available, as existing CDTs primarily target the cancer immune microenvironment. We have reported that TAZ, a co-transcription factor, is upregulated and activated in HCC. This study investigates TEAD, a transcription factor known to interact with TAZ.
Method: HCC was induced in mice through hydrodynamic tail vein injection of Sleeping Beauty plasmids carrying TAZ-S89A, TAZ-S89A-S51A, cMet, and CTNNB1(bCat)-S45Y. We utilized the CRISPR interference (CRISPRi) system to knock down Tead1, Tead2, Tead3, or Tead4 in HCC, using dead Cas9 transgenic mice and plasmids with gRNA for each Tead to evaluate the effects on HCC development and survival. We also analyzed the correlation between TEAD1-4 expression and patient survival in the TCGA-LIHC cohort.
Results: Overexpression of TAZ via HTVI of TAZ-S89A plasmid alone induced HCC, while TAZ-S89A-S51A, unable to interact with TEADs, did not. CRISPRi-mediated knockdown of Tead2 significantly suppressed HCC development in both TAZ-S89A-driven and cMet+bCat-S45Y-driven models. Knockdown of any Tead prolonged survival in mice with cMet+bCat-S45Y-driven HCC. TCGA-LIHC cohort analysis revealed that lower expression of TEAD2 or 4 predicts better overall survival, and lower expression of TEAD2 or 3 predicts better recurrence-free survival. Pan-TEAD inhibitor significantly suppressed HCC development in the Met+bCat-S45Y model.
Conclusion: TEAD inhibitors are suggested as a novel therapeutic option for HCC, directly targeting cancer cells.

P-153
10023

Myositis Induced by an Immune Checkpoint Inhibitor in a Hepatocellular Carcinoma Patient with Primary Biliary Cirrhosis: A Case Report

Naoya Tsuzuki[1], Kaho Miyazaki[1], Takumi Sugiyama[1], Yasuki Hatayama[1], Daisuke Murakami[1], Yukiko Shima[1], Harutoshi Sugiyama[1], Takayoshi Nishino[1], Rie Kuroda[2], Sho Wakou[2], Hiroshi Yoshizawa[2], Makoto Arai[1]
[1]Department of Gastroenterology, Tokyo Women's Medical University Yachiyo Medical Center, Japan, [2]Department of Neurology, Tokyo Women's Medical University Yachiyo Medical Center, Japan

A 74-year-old man was diagnosed with primary biliary cirrhosis (PBC) after a liver biopsy in 2013. In 2021, hepatocellular carcinoma (HCC) was detected, so he received partial resection of the liver. Then, he received transcatheter arterial chemoembolization for recurrent HCC. Because of multiple intrahepatic recurrences of HCC, he received chemotherapy (atezolizumab 1200 mg/body and bevacizumab 15 mg/kg) in 2024. On Day 9, after administration of the chemotherapy, liver function and the serum creatine phosphokinase (CK) value normalized (47 U/L). On Day 12, he suddenly developed a fever but no treatment was sought. On Day 14, he became immobile and was urgently hospitalized. There was no paralysis, but tenderness was present in the left upper arm and bilateral proximal lower extremities. Laboratory testing revealed elevated serum CK (4568 U/L). The CK-MB value was not elevated. He was diagnosed with myositis due to immune-related adverse events (irAE) and began steroid therapy (1.0 mg/kg per day). The CK value decreased rapidly, and subjective symptoms, such as tenderness, disappeared, but fatigue and poor appetite persisted. Liver function also did not improve to the level observed before administration of chemotherapy. The course of the disease was complicated by hepatic encephalopathy and infection, and the patient died of liver failure on Day 78.
This case showed a sudden onset of myositis due to irAE with no symptoms or normal laboratory findings appeared until 4 days before the onset of symptoms. Whether PBC may have influenced the outcome of this case remains to be determined.

P-154
10067

A Case of Unresectable Hepatocellular Carcinoma Complicated by Cerebral Hemorrhage after Combined Therapy with Atezolizumab and Bevacizumab

Tamami Abe, Hidekatsu Kuroda , Takuya Watanabe, Hiroaki Abe, Kenji Yusa, Yudai Fujiwara, Hiroki Sato, Akiko Suzuki, Kei Endo, Yuichi Yoshida, Takayoshi Oikawa, Keisuke Kakisaka, Kei Sahara, Akio Miyasaka, Takayuki Matsumoto
Division of Gastroenterology and Hepatology, Department of Internal medicine, Iwate Medical University, Iwate, Japan

An BCLC-C 80-year-old man received ATZ+BEV from February 2024. After 6 courses, the patient experienced floating dizziness and urgently sought medical attention. JCS-1, GCS E4V5M6=16, Body temperature 36.3C, blood pressure 144/77 mmHg, SpO2 97% (room air). WBC 4730 /μL, PLT 15100 /μL, PT-INR 1.07, Na 139 mmol/L, K 4.3 mmol/L, Cl 104 mmol/L, blood glucose 127 mg/dL. Head CT suspected minute hemorrhage in the right thalamus and basal ganglia showing pinpoint high absorption areas. Based on imaging diagnosis, cerebral hemorrhage was confirmed. Follow-up CT on the following day showed a tendency for the hemorrhage to shrink, with improvement in subjective symptoms. Brain MRI on the 8th hospital day revealed cerebral microbleeds, but no new hemorrhage or expansion of the hemorrhage sites was observed. The patient is under rehabilitation and observation. Bleeding events as adverse events are considered highly related to BEV, with mechanisms such as inhibition of interactions between endothelial cells and platelets necessary for vascular homeostasis and inhibition of wound healing by neovascularization. In this case, the patient had no hypertension, smoking history, or history of antiplatelet or anticoagulant drug use. Although no cerebral aneurysm was observed in the pre-treatment brain MRI. The Cardio Ankle Vascular Index after the onset of cerebral hemorrhage was 9.8 on both sides (reference value ~8.9), suggesting arteriosclerosis. At the age of 86, age-related arteriosclerosis was considered a bleeding risk. Being elderly itself could be a bleeding risk and should be considered.

P-155
10072

A Case of Duodenal Bleeding from Invasion of Lymph Node Metastasis during Combination Therapy with Atezolizumab and Bevacizumab for Hepatocellular Carcinoma

Kyoko Hoshikawa, Fumiya Suzuki, Keita Maki, Tomohiro Katsumi, Hiroaki Haga, Yoshiyuki Ueno
Department of Gastroenterology, Yamagata University, Yamagata, Japan

Case: 62-year-old male. [Chief complaint] Bloody stool.
Medical History: The patient was diagnosed with multiple hepatocellular carcinomas (HCC), portal vein invasion, and multiple lung metastases in September 2023. He started systemic chemotherapy with atezolizumab and bevacizumab, has received a total of 11 courses so far. In June 2024, he visited the emergency room because of the bloody stools and was admitted to the hospital.
Examination findings: Laboratory tests showed anemia (Hb 9.4 g/dL), elevated WBC (14,670/μL), and increased CRP (6.84 mg/dL). CT scan revealed a mass near the duodenum, likely a lymph node metastasis, compressing the duodenal wall. Upper GI endoscopy confirmed an A2 stage ulcer on the duodenal bulb's posterior wall, although no active bleeding was seen.
Clinical Course: Based on the above history and lab results, gastrointestinal bleeding was suspected due to duodenal invasion by metastatic lymph nodes from HCC. Initial management included fasting and PPI therapy to stabilize the patient and promote ulcer healing. A vascular embolization procedure targeting the metastatic lymph node near the duodenum was performed on the sixth hospital day, successfully controlling the bleeding. Following embolization, the patient's condition improved, and he was discharged on the 22nd day of hospitalization.
Discussion: Combination therapy using atezolizumab and bevacizumab effectively treats unresectable HCC, but bevacizumab has poses risks, notably bleeding. This case illustrates bleeding from duodenal invasion by metastatic lymph nodes during treatment, necessitating vascular embolization. Vigilance for such complications is crucial during bevacizumab therapy to ensure timely management and optimize patient outcomes.

P-156
10076

A Case of Hepatic Hemangiosarcoma Followed by Long-term Imaging

Takayuki Kogure, Mari Satoh, Morihisa Hirota, Atsuko Takasu, Akinobu Koiwai, Tomofumi Katayama, Yuki Miyashita, Nana Inomata, Yuka Yamazaki, Jun Yamada, Kohei Igarashi, Kennichi Satoh
Division of Gastroenterology, Tohoku Medical and Pharmaceutical University, Sendai, Japan

Background: Hepatic angiosarcoma is associated with a poor prognosis due to rapid growth, resulting in mortality within six months. We report a case of hepatic angiosarcoma that was followed without treatment for over three years.
Case Presentation: A 77-year-old female presented to our department to evaluate multiple liver nodules that had been observed to enlarge gradually. Approximately one-year prior, incidental liver nodules were identified during an ultrasound conducted as routine examinations for hypercholesterolemia. Despite a comprehensive assessment including CT/MRI, the diagnosis remained unconfirmed. CT imaging demonstrated multiple nodules, ranging in size from 1 to 3 cm, in the bilateral liver lobes. The nodules showed a weak enhancement peripherally in the late phase. Laboratory tests showed no abnormality in tumor markers or evidence of chronic liver diseases. A percutaneous needle biopsy revealed atypical endothelial cells with irregular nuclei observed in the sinusoidal wall, accompanied by distortion of hepatic cords. The atypical cells expressed CD31 and ERG, and we diagnosed angiosarcoma. She opted for conservative management without chemotherapy. During follow-up, the nodules' contrast pattern changed to a typical appearance of hepatic angiosarcomas, with enhancement gradually spreading from the margins toward the center. The tumors progressed to occupy most of the liver after three years. She presented with sudden abdominal pain, and a tumor rupture was found, causing hemorrhagic shock and death.
Discussion: The case of hepatic angiosarcoma followed for more than three years without treatment could document changes in images over time. This finding contributes to our understanding of hepatic angiosarcoma.

P-157
10106

A Case of Hepatic Focal Nodular Hyperplasia after Liver Transplantation

Kenichi Nakamura, Yoshinori Ozono, Yuri Komaki, Hisayoshi Iwakiri, Satoru Hasuike, Kenji Nagata, Hiroshi Kawakami
Division of Gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan

A 72-year-old man was diagnosed with hepatocellular carcinoma (HCC) in 2018 and underwent transarterial chemoembolization and proton beam therapy in 2019. Subsequently, he developed liver failure and underwent liver transplantation (LT) in February 2020. CT 1 year after LT showed a 10 mm hyperattenuating lesion in the liver, but did not show wash out in the portal venous and equilibrium phase. CT 2 years after LT showed known hyperattenuating lesion had increased in size. B-mode ultrasonography (US) showed hypoechoic nodule about 10 mm in diameter. Contrast-enhanced US showed the nodule is hyperattenuating in the early vascular phase, and no defect in the Kupffer phase. Since there was no increase in tumor markers (AFP/PIVKA-II/CEA/CA19-9), focal nodular hyperplasia (FNH) or hepatocellular adenoma were suspected. EOB-MRI 3 years after LT showed known lesion was hyperintensity in the arterial phase with no wash out in the portal venous and equilibrium phase, but the lesions showed hypointensity inside and hyperintensity outside in the hepatobiliary phase. Therefore, HCC could not be ruled out, and a liver tumor biopsy was performed in July 2023. Histopathology showed increased small hepatocytes with high N/C ratio, increased number of small bile ducts, small muscular vessels, and dilated sinusoids, but no cell atypia. The central scar was not evident, but some areas showed mild fibrosis with inflammatory cell infiltration. Immunostaining showed that the tumor was positive for glutamine synthetase and C reactive protein, and negative for serum amyloid A. Based on these findings, the hepatic tumor was diagnosed with FNH.

Poster Session

P-158
10137

A Case of Scirrhous Hepatocellular Carcinoma Discovered after Combined Immunotherapy for Hepatocellular Carcinoma

Yuta Maruki[1], Takeshi Takamoto[2], Mao Okada[1], Chigusa Morizane[1], Hideki Ueno[1], Akinori Miyata[3], Takahiro Mizui[3], Daisuke Ban[3], Satoshi Nara[3], Minoru Esaki[3], Nobuyoshi Hiraoka[4], Takuji Okusaka[1]
[1]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, [2]Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, the University of Tokyo, [3]Hepatobiliary and Pancreatic Surgery Division, National Cancer Center Hospital, [4]Division of Pathology & Clinical Laboratories, National Cancer Center Hospital, Japan

Background: Scirrhous hepatocellular carcinoma (SHC) is a rare variant of hepatocellular carcinoma (HCC) comprising approximately 1-5% of primary liver cancers. However, the efficacy of combined immunotherapy for SHC remains unclear.
Case: A 73-year-old woman with alcoholic cirrhosis presented with a tumor in segment 1 and papillary growth in the common bile duct, which was diagnosed as HCC via biopsy. Liver function test results showed Child-Pugh B (7), with an ALBI score of -1.262. Liver function worsened, liver resection was difficult, and initial treatment included 11 cycles of atezolizumab and bevacizumab. Subsequently, she received MRI-synchronized radiotherapy (40 Gy/5 Fr) as second-line therapy. After nine months, a 20 mm mass in segment 7 was detected on CT, showing early enhancement consistent with HCC. The patient underwent a partial hepatectomy. The surgical specimen revealed cirrhosis and a 20 mm lobular, firm, nodular tumor with a pale brown, slightly greenish cut surface beneath the liver capsule. Histologically, the tumor showed radial fibrosis from the center to the margins, suggesting an atypical HCC. Special stains for CK7 and CD68 were also positive. The differential diagnosis tested negative for the DNAJB1-PRKACA fusion gene using FISH, confirming SHC.
Conclusion: SHC typically affects men with cirrhosis in their 60s. In this case, SHC was diagnosed based on an examination of the resected specimen, despite the initial diagnostic challenges.

Better Health,
Brighter Future

タケダは、世界中の人々の健康と、
輝かしい未来に貢献するために、
グローバルな研究開発型のバイオ医薬品企業として、
革新的な医薬品やワクチンを創出し続けます。

1781 年の創業以来、受け継がれてきた価値観を大切に、
常に患者さんに寄り添い、人々と信頼関係を築き、
社会的評価を向上させ、事業を発展させることを日々の行動指針としています。

武田薬品工業株式会社
www.takeda.com/jp

Takeda

NK
Speciality, Biosimilar & Generic

より多くの、必要としている患者さんに届けたい。

日本化薬のバイオシミラー製品ラインナップ

薬価基準収載

ヒト型抗ヒトTNFαモノクローナル抗体製剤 生物由来製品・劇薬・処方箋医薬品*
アダリムマブ（遺伝子組換え）［アダリムマブ後続4］製剤
アダリムマブBS皮下注
20mgシリンジ0.2mL・40mgシリンジ0.4mL・80mgシリンジ0.8mL「CTNK」
40mgペン0.4mL・80mgペン0.8mL「CTNK」
Adalimumab BS Subcutaneous Injection
20mg Syringe 0.2mL・40mg Syringe 0.4mL・80mg Syringe 0.8mL「CTNK」
40mg Pen 0.4mL・80mg Pen 0.8mL「CTNK」
提携先
セルトリオン・ヘルスケア・ジャパン株式会社
東京都中央区新川一丁目16番3号住友不動産茅場町ビル3階

抗悪性腫瘍剤/抗VEGFヒト化モノクローナル抗体 生物由来製品・劇薬・処方箋医薬品*
ベバシズマブ（遺伝子組換え）［ベバシズマブ後続4］製剤
ベバシズマブBS点滴静注
100mg・400mg「CTNK」
Bevacizumab BS for I.V. Infusion 100mg・400mg「CTNK」
提携先
セルトリオン・ヘルスケア・ジャパン株式会社
東京都中央区新川一丁目16番3号住友不動産茅場町ビル3階

G-CSF製剤 処方箋医薬品*
フィルグラスチム（遺伝子組換え）［フィルグラスチム後続2］製剤
フィルグラスチムBS注
75μg・150μg・300μgシリンジ「NK」
Filgrastim BS Inj. 75μg・150μg・300μg Syringe「NK」

抗HER2ヒト化モノクローナル抗体 抗悪性腫瘍剤 生物由来製品・処方箋医薬品*
トラスツズマブ（遺伝子組換え）［トラスツズマブ後続1］製剤
トラスツズマブBS点滴静注用
60mg・150mg「NK」
Trastuzumab BS for I.V. Infusion 60mg・150mg「NK」

抗ヒトTNFαモノクローナル抗体製剤 生物由来製品・劇薬・処方箋医薬品*
インフリキシマブ（遺伝子組換え）［インフリキシマブ後続1］製剤
インフリキシマブBS点滴静注用100mg「NK」
Infliximab BS for I.V. Infusion 100mg「NK」

*注意－医師等の処方箋により使用すること

製造販売元 日本化薬株式会社
東京都千代田区丸の内二丁目1番1号

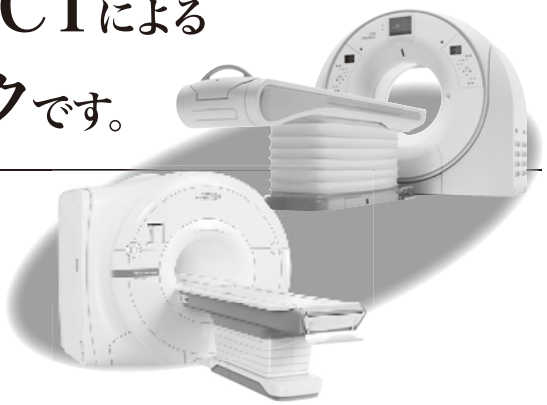
文献請求先及び問い合わせ先
日本化薬 医薬品情報センター
0120-505-282

日本化薬 医療関係者向け情報サイト
https://mink.nipponkayaku.co.jp/

'23.12作成

各種保険取扱

メディカルスキャニングはMRI・CTによる画像検査・診断の専門クリニックです。



「すぐ検査を受けたい」「検査・診断をしてほしい」という
患者様・医療機関の皆様の想いを実現し、
最適な医療の普及に貢献することを目指しています。

1 駅からすぐ
各クリニックはいずれも駅から近くにあります。

2 引っ越しても大丈夫
各クリニックはネットワークされています。
患者さんが希望すれば、将来転居し新居の近くのメディカルスキャニングを利用した場合も過去画像との比較が可能です。

3 HUB機能
患者さんが過去に他院からの紹介で、メディカルスキャニングを受診した際の過去画像で比較可能な場合があります。（要患者承諾）

4 毎日診療
正月の3が日を除く毎日診療しています。
平日・土曜は朝8時半から夜8時まで。
日曜・祝日も診療しています。
＊診療時間の詳細はお問い合わせください。

5 保険診療
各種健康保険に対応しています。

6 3テスラMRI
3テスラMRIなど最新鋭の設備を備え、高分解能、低被ばく（CT）、迅速で高品質の報告書を心がけています。
＊機器、設備の詳細はお問い合わせください。

7 信頼と実績
年間60万件超の画像検査・診断症例数。
大学病院や基幹病院からの検査・診断も多数受けています。

8 撮影条件等
撮影に関する細かいご指定がある場合もご相談ください。

9 当日検査、画像診断
当日検査、当日画像診断報告書のご提供も可能です。ご相談ください。

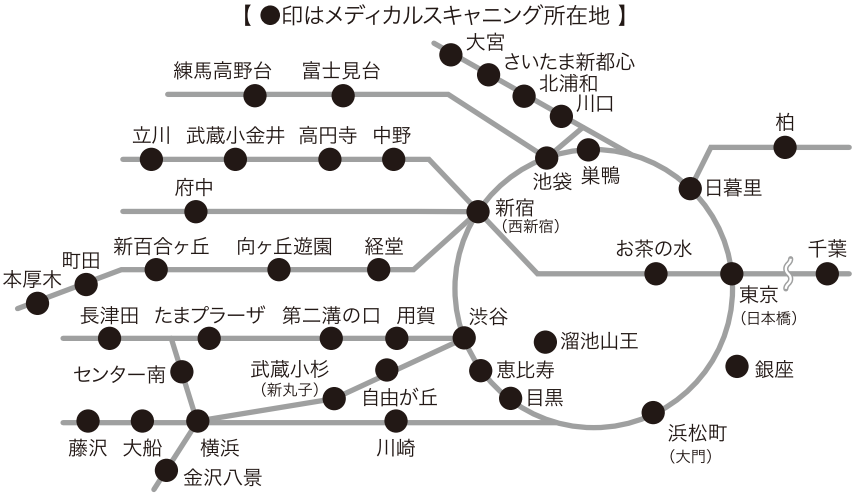
10 後方支援医療機関も充実
後方支援医療機関も充実しており、必要な場合主治医の先生とご相談の上、利用できる体制も整っています。

MEDICAL SCANNING
メディカルスキャニング

メディカルスキャニングは42箇所あり、いずれも最寄駅から徒歩0～5分（恵比寿7分）の駅近くにあります。
診療時間は朝8:30～夜8:00 土日・祝日も診療しています。
※診療時間は施設によって異なりますのでお問い合せの上ご確認下さい。

お問合せ・ご予約は（全クリニック共通）
TEL：03-5778-2905

【 ●印はメディカルスキャニング所在地 】



https://www.medicalscanning.net

サイエンスを通じて、
患者さんの人生に違いをもたらす™

深刻な病と闘う患者さんに革新的な医薬品を開発し、提供する。私たちは、この使命を胸に、
世界中であくなき挑戦を続けます。ひとりでも多くの患者さんに、新たな希望をお届けするために。
患者さんの人生に違いをもたらすイノベーションを起こす。それが、私たちの務めです。

Bristol Myers Squibb™
ブリストル マイヤーズ スクイブ

For Hyperlipidemia

PARMODIA® XR TABLETS 0.2mg・0.4mg

Prescription drug-Prescription by physician is required
(Pemafibrate Extended Release tablets) NHI drug price listing

This content here is not intended to recommend the use of pemafibrate in countries where it is not approved.

Please refer to the package insert for indications, dosage and administration, and precautions for use including contraindications.

Manufactured and distributed by :
Kowa Company, Ltd.
4-14, Nihonbashi-Honcho 3-Chome, Chuo-ku, Tokyo, JAPAN

24.3

CYRAMZA®
(ramucirumab)

抗悪性腫瘍剤 ヒト型抗VEGFR-2注) モノクローナル抗体
生物由来製品、劇薬、処方箋医薬品*

サイラムザ® 点滴静注液 100mg
点滴静注液 500mg

CYRAMZA® Intravenous Injection ラムシルマブ(遺伝子組換え)注射液

注)VEGFR-2: Vascular Endothelial Growth Factor Receptor-2(血管内皮増殖因子受容体2)
*注意ー医師等の処方箋により使用すること

薬価基準収載

「効能又は効果」、「用法及び用量」、「警告・禁忌を含む注意事項等情報」等については電子添文をご参照ください。

PP-RB-JP-7143
2022年10月作成

製造販売元〈文献請求先及び問い合わせ先〉
日本イーライリリー株式会社
〒651-0086 神戸市中央区磯上通5丁目1番28号

Lilly Answers リリーアンサーズ
日本イーライリリー医薬情報問合せ窓口
www.lillymedical.jp

(医療関係者向け)
0120-360-605※1
受付時間 月曜日～金曜日 8:45～17:30※2
※1 通話料は無料です。携帯電話からでもご利用いただけます。
尚、IP電話からはフリーダイヤルをご利用できない場合があります。
※2 祝祭日および当社休日を除きます。

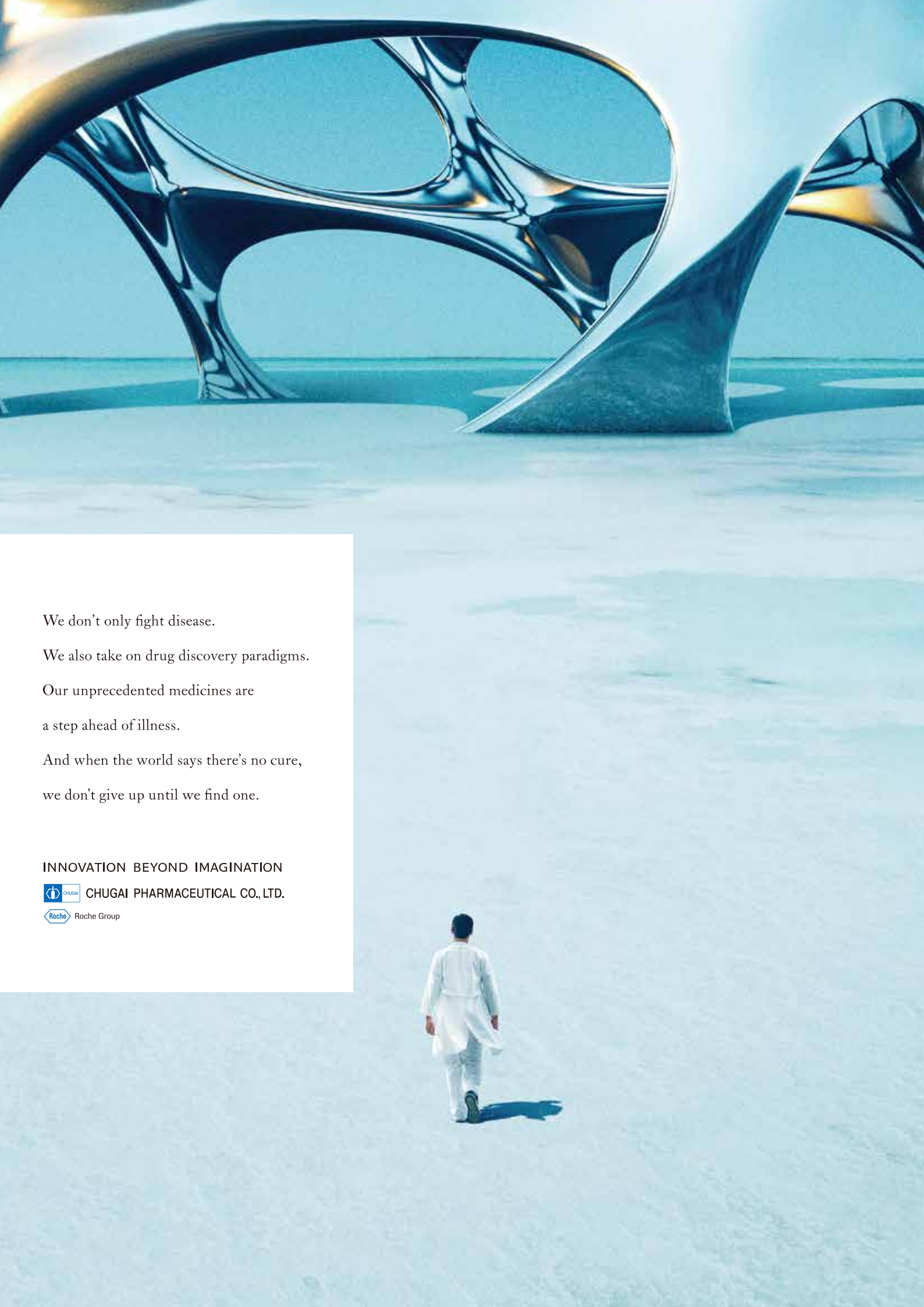
Lilly

患者様の想いを見つめて、薬は生まれる。

顕微鏡を覗く日も、薬をお届けする日も、見つめています。
病気とたたかう人の、言葉にできない痛みや不安。生きることへの希望。
私たちは、医師のように普段からお会いすることはできませんが、
そのぶん、患者様の想いにまっすぐ向き合っていたいと思います。
治療を続けるその人を、勇気づける存在であるために。
病気を見つめるだけではなく、想いを見つめて、薬は生まれる。
「ヒューマン・ヘルスケア」。それが、私たちの原点です。

ヒューマン・ヘルスケア企業　エーザイ

AFUTUREFREEOFLF
GlobalAlliance
エーザイはWHOのリンパ系フィラリア病制圧活動を支援しています。



We don't only fight disease.

We also take on drug discovery paradigms.

Our unprecedented medicines are

a step ahead of illness.

And when the world says there's no cure,

we don't give up until we find one.

INNOVATION BEYOND IMAGINATION

CHUGAI PHARMACEUTICAL CO., LTD.

Roche Group

私たちのイノベーションを、
待っている人がいる。

ギリアドは、信じています。
不可能は、不可能ではない。
まだ見ぬ可能性の源であると。
そんな思いで私たちはHIV、肝炎、
炎症性疾患、そしてがんなどの疾病に
革新的なアプローチで挑み、患者さんのより良い生活を
実現するための治療薬を開発してきました。
新型コロナウイルス感染症の流行にもいち早く対応し、
世界で最初に承認された抗ウイルス薬を開発。
不可能へと挑む勇気、そして患者さんを想う強い気持ちをもって、
一丸となり新たな可能性を生み出してきました。
多くの患者さん、それを支える人たちを守るという強い決意のもと、
日本法人を立ち上げて、10年を越えました。
まだまだ、私たちの創薬を待つ人がいる。
これからも、この日本で、一緒に。
イノベーションを起こし続けることを誓います。
私たちは、ギリアド・サイエンシズ。
不可能は不可能ではないと、証明するために。

AstraZeneca

anti cancer drug /
human monoclonal antibody that binds to the PD-L1 protein

Listed in NHI drug price standard

IMFINZI® Injection 120mg Injection 500mg

Durvalumab (Genetical Recombination) injection, for intravenous use

Biological products, Powerful drug, Prescription - only drug (Caution - Use only as directed by a physician, etc.)
The drugs to be subjected to Optimal Clinical Use Guidelines

anti cancer drug /
human monoclonal antibody that targets the activity of CTLA-4

Listed in NHI drug price standard

IMJUDO® Injection 25mg Injection 300mg

Tremelimumab (Genetical Recombination) injection, for intravenous use

Biological products, Powerful drug, Prescription - only drug (Caution - Use only as directed by a physician, etc.)

Please refer to package insert for indications, dosage and administration, precautions including warnings, contraindications, and others.

Marketing Authorization Holder / Distributor
Where to request for materials
AstraZeneca K.K.
3-1 Ofukacho, Kita-ku, Osaka
Toll free telephone service：0120-189-115
(Medical Information Center)

Created: March, 2024