
The Asian Pacific Association for the Study of the Liver
APASL Oncology 2023
In Search of Silver Bullet for HCC
Program & Abstracts
Term: October 27-28, 2023
City: Sendai, Japan
Venue: Hotel Metropolitan Sendai
President: Yoshiyuki Ueno, MD. FAASLD.
Professor and Chairman,
Department of Gastroenterology, Faculty of Medicine, Yamagata University, Japan
www.apasl-oncology2023.org
Supported by JSH

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APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Hybrid Meeting (Onsite-Venue: Hotel Metropolitan Sendai)

October 27- 28, 2023

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Welcome Message

Dear Colleagues,

On behalf of the Organizing Committee, it gives us great pleasure to invite you to Asian Pacific Association for the Study of the Liver APASL Oncology 2023 Sendai, which will be held on October 27-28 2023 in Sendai, Japan. We are delighted to welcome you to the attractive city of Sendai.

The scientific program will consist of invited lectures, plenary sessions, symposia, and free papers on significant developments on the theme of “In Search of Silver Bullet for HCC”. The program will also provide the latest information and fresh ideas of Oncology for hepatologists. The conference encouraged the submission of abstracts on research for oral and poster presentations through the conference and received more than 150 free papers. We would appreciate your submission which will stimulate active discussions. 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.

In spite of the confusion due to the COVID-19 Pandemic, we have received outstanding abstracts from APASL colleagues. We are so grateful for our colleagues, administrative office and patients. Finally, we have achieved cutting-edge programs as APASL single topic conference.
We look forward to welcoming you in Sendai.

With warmest regards,

Yoshiyuki Ueno, MD. FAASLD.
President, APASL Oncology 2023 Sendai
Professor and Chairman,
Department of Gastroenterology,
Faculty of Medicine, Yamagata University, Japan

Invited Guest Speakers/Chairs/Scientific Committee

Invited Guests/Speakers/Chairs/Scientific Committee from Overseas

Dr. Henry L.Y. Chan (China)
Dr. Darrell Crawford (Australia)
Dr. A. Kadir Dokmeci (Turkey)
Dr. Gregory J. Gores (USA)
Dr. Ji-Dong Jia (China)
Dr. Jia-Horng Kao (Taiwan)
Dr. George K. K. Lau (China)
Dr. Cosmas R.A. Lesmana (Indonesia)
Dr. Han-Chieh Lin (Taiwan)
Dr. Mindie H. Nguyen (USA)
Dr. Tushar Patel (USA)
Dr. Shiv K. Sarin (India)
Dr. Barjesh C. Sharma (India)
Dr. Jose Sollano (Philippines)
Dr. Tawesak Tanwandee (Thailand)
Dr. Lai Wei (China)
Dr. Grace L.H. Wong (China)
Dr. Man-Fung Yuen (China)

In alphabetical order

Invited Guests/Speakers/Chairs/ Scientific Committee from Japan

Dr. Kazumichi Abe
Dr. Takehiro Akahane
Dr. Nobuhisa Akamatsu
Dr. Norio Akuta
Dr. Kuniaki Arai
Dr. Makoto Arai
Dr. Yasuhiro Asahina
Dr. Yoshinari Asaoka
Dr. Masanori Atsukawa
Dr. Kazuaki Chayama
Dr. Makoto Chuma
Dr. Akihiro Deguchi
Dr. Hirotoshi Ebinuma
Dr. Hirayuki Enomoto
Dr. Nobuyuki Enomoto
Dr. Hideki Fujii
Dr. Masafumi Fujita
Dr. Junji Furuse
Dr. Hiroaki Haga
Dr. Kiyoshi Hasegawa
Dr. Etsuro Hatano
Dr. Yoichi Hiasa
Dr. Hayato Hikita
Dr. Keisuke Hino
Dr. Naoki Hiramatsu
Dr. Atsushi Hiraoka
Dr. Masao Honda
Dr. Akio Ido
Dr. Hiroko Iijima
Dr. Yuji Iimuro
Dr. Masafumi Ikeda
Dr. Tadashi Ikegami
Dr. Kenichi Ikejima
Dr. Kento Imajo
Dr. Jun Inoue
Dr. Hiroyuki Isayama
Dr. Masatoshi Ishigami
Dr. Toru Ishikawa
Dr. Jun Itakura
Dr. Kiyoaki Ito
Dr. Takanori Ito
Dr. Yoshihito Itoh
Dr. Shinji Itoh
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Dr. Satoru Joshita
Dr. Tatehiro Kagawa
Dr. Masaki Kaibori
Dr. Eiji Kakazu
Dr. Keisuke Kakisaka
Dr. Satoru Kakizaki
Dr. Tatsuo Kanda
Dr. Tatsuya Kanto
Dr. Naoya Kato
Dr. Tomohiro Katsumi
Dr. Norifumi Kawada
Dr. Takumi Kawaguchi
Dr. Yusuke Kawamura
Dr. Miwa Kawanaka
Dr. Tomokazu Kawaoka
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Dr. Shigehiro Kokubu
Dr. Atsumasa Komori
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Dr. Hirohisa Yano
Dr. Hiroshi Yatsuhashi
Dr. Osamu Yokosuka
Dr. Hitoshi Yoshiji
Dr. Kengo Yoshimitsu
Dr. Sachiyo Yoshio
Dr. Hiroshi Yotsuyanagi

In alphabetical order

Organizing Committee

Local Organizing Committee

Honorary President: Dr. Masao Omata

President: Dr. Yoshiyuki Ueno

Vice President: Dr. Masatoshi Kudo, Dr. Naoya Kato

Treasurer: Dr. Shuichiro Shiina

Vice-Treasurer: Dr. Hidekatsu Kuroda, Dr. Jun Inoue

Secretary General: Dr. Hiroaki Haga

Committee: Dr. Masayuki Kurosaki
Dr. Yasuhito Tanaka
Dr. Hitoshi Yoshiji
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Dr. Ryosuke Tateishi

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Chairman of Steering Committee: Dr. Shiv Kumar Sarin (India)

President: Dr. Shuichiro Shiina (Japan)

Immediate Past President: Dr. Han-Chieh Lin (Taiwan)

President Elect: Dr. Lai Wei (China)

Secretary General-cum-Treasurer: Dr. Manoj K Sharma (India)

Past Presidents:

Dr. Laurentius A. Lesmana (Indonesia)
Dr. Jose Sollano (Philippines)
Dr. Masao Omata (Japan)
Dr. Dong Jin Suh (Korea)
Dr. George K. K. Lau (China)
Dr. Ji Dong Jia (China)
Dr. Teerha Piratvisuth (Thailand)
Dr. Jia-Horng Kao (Taiwan)
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Dr. Diana A. Payawal (Philippines)
Dr. Rino Gani (Indonesia)
Dr. Tawesak Tanwandee (Thailand)
Dr. Jin Mo Yang (Korea)

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President: Dr. Shuichiro Shiina (Japan)
Immediate Past President: Dr. Han-Chieh Lin (Taiwan)

President Elect: Dr. Lai Wei (China)

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

Category \ Term	Early Bird until July 31, 2023	Pre-Registration October 20, 2023	On Site
APASL Member	JPY 25,000	JPY 30,000	JPY 35,000
Non-Member	JPY 30,000	JPY 35,000	JPY 40,000
Trainee / Resident	JPY 20,000	JPY 25,000	JPY 30,000
Accepted Abstract Submitter	JPY 25,000	JPY 30,000	JPY 35,000
Student	JPY 5,000	JPY 5,000	JPY 5,000
Accompanying Person	JPY 5,000	JPY 5,000	JPY 5,000

JPY=Japanese Yen

*APASL Members who have paid 2023 Membership Fee can apply for discounted registration fee.

Online Participation (Style: Zoom Webinar)

- The conference program will be presented as a hybrid style meeting.
- Attendants are able to enter the webinar through Zoom https://zoom.us/join with the ID and Password of which they have been informed by the conference secretariat. * For Speakers/Chairs, the secretariat sends an individual invitation link to enter the webinar.
- The lectures will be delivered live or by recorded video. After the presentation, the discussion (Q&A) time will be held according to the moderator's instructions. Online viewers are able to send textual questions to the Q&A column, and the onsite participants may ask questions using the microphone in the conference room. We anticipate your active discussions.
- After the conference term, the recorded lectures and discussion will be distributed on-demand from the presentation page of APASL Oncology 2023 Website http://www.apasl-oncology2023.org/
  The viewing period of the on-demand presentation is scheduled to be from November 1, 2023 through November 30, 2023. The secretariat will receive the questions by e-mail during the on-demand delivery period and will forward them to each speaker.

[Precautions]

- The organizer cannot handle problems such as computer operation, internet connection, video and audio connection. Please solve such problems by yourself. We recommend the following environment.
  -We would appreciate it if you could use a PC with as much memory as possible (CPU i5 or more, memory 8 Giga or more).
  -Please connect to the Internet via a wired LAN line as much as possible.
- To transfer or share the ID and password, recording of screens and images is strictly prohibited.
- The internet fee at this online conference will be borne by each attendant.

We cordially solicit your understanding and cooperation.

Onsite Registration/PC Pre-view Hours

October 27 (Friday)	7:30-18:00 (JST)
October 28 (Saturday)	7:30-16:00 (JST)

Venue (Hybrid Style Meeting)

HOTEL METROPOLITAN SENDAI

Address:	1-1-1, Chuo Aoba-ku Sendai city Miyagi, Japan
Tel:	+ 81-22-268-2525
URL:	https://sendai.hotel-metropolitan.com/stay/index.html

Location:

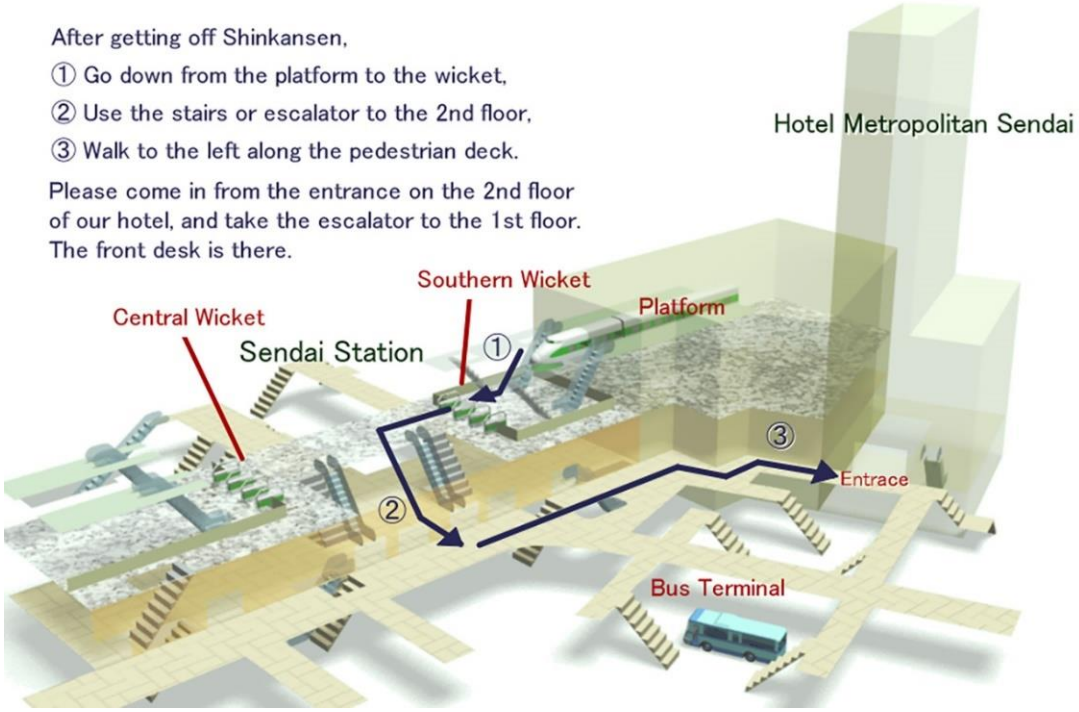
Domestic flight: 1 hour. flight from Tokyo Haneda Airport to Sendai Airport

International flight: There are direct flights from Seoul, Shanghai, Dalian, Beijing and Taipei to Sendai Airport.

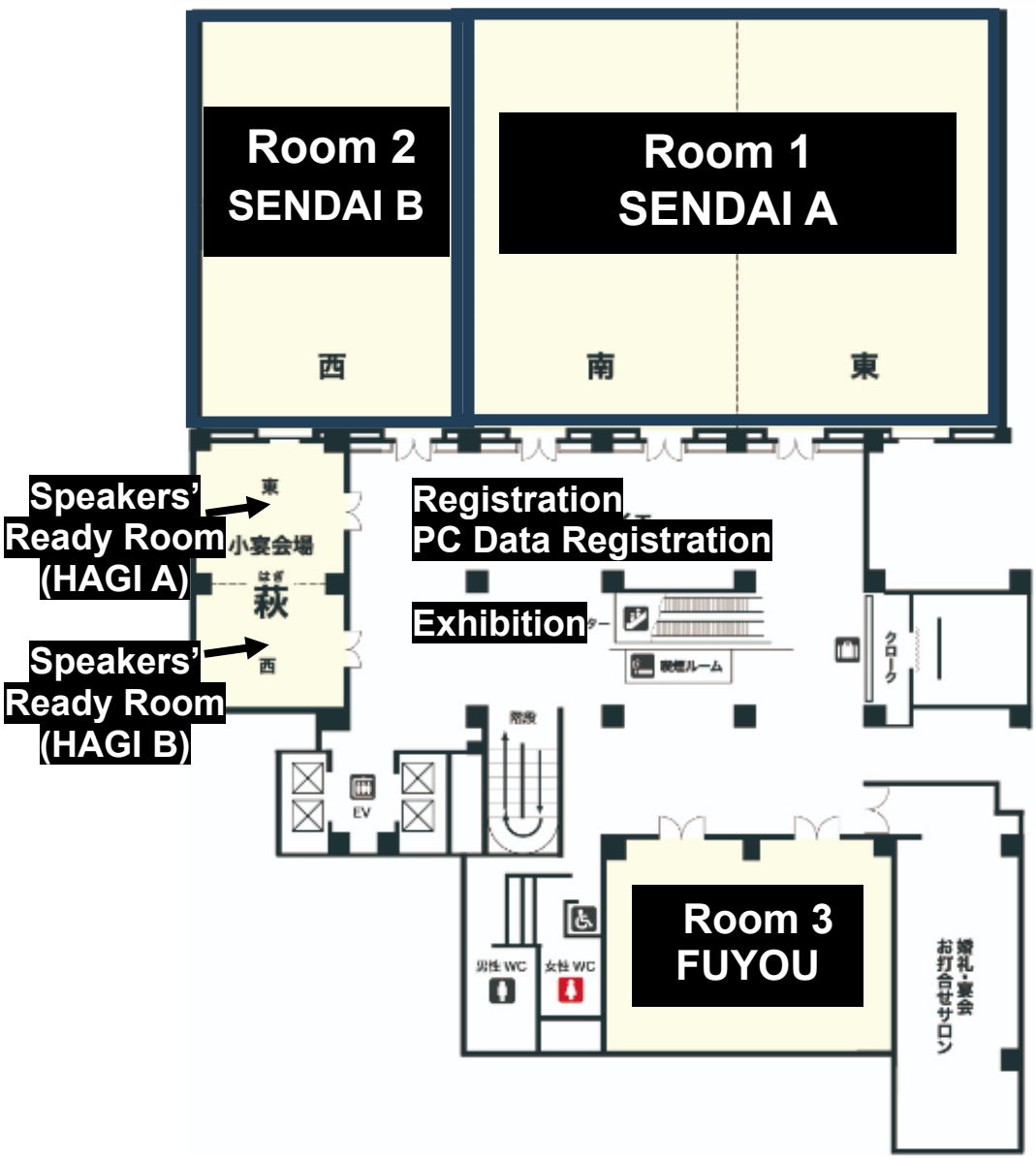
The time table is available at following URL.

https://www.sendai-airport.co.jp/flight/intl-monthly.html

From Sendai Airport to the venue, 40 min. ride by train / 35 min. ride by Taxi



Floor Plan: 4F, HOTEL METROPOLITAN SENDAI



Room 1 "SENDAI A", 4th Floor: Lectures, Workshops
Room 2 "SENDAI B", 4th Floor: Lectures, Workshops, Poster Sessions
Room 3 "FUYOU", 4th Floor: Poster Sessions
Registration: Foyer, 4th Floor
Speakers/Chairs Ready Room: "HAGI", 4th Floor
Cloak: Foyer, 4th Floor
PC Preview Desk: Foyer, 4th Floor

About infection prophylaxis

We hereby present our guidelines on infection measures for participants and cordially request your understanding and cooperation on this matter.

- We recommend that you wear your mask when visiting the venue.
- Anyone who records a fever will be advised not to enter the venue.
- Periodical indoor ventilation will be employed in the venue.

Instruction for Oral Presentation

The conference program will be presented as a hybrid style meeting.

- An invitation email containing information about the login will be sent to the presenters/moderators through the Zoom system. The login URL will be included in the invitation email.
- We would appreciate it if you could conduct a test connection ahead of the conference.
- Presentation time:
  - Workshop sessions' each presentation time is 12 minutes (within 9 minutes presentation, 3 minutes discussion).
  - Onsite Poster Session's each presentation time is 6 minutes (within 4 minutes presentation, 2 minutes discussion).

[For those who will participate at the onsite venue]

- Please complete your registration of presentation data at the Data Pre-View Desk until 1 hour before your presentation time.
- 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. Please operate the slides by yourself. Please note that the presenter tool is not available.

[For those who will attend online]

- Please join Zoom at least 20 minutes before your session begins.
- Please turn on the microphone and the camera only when you are speaking.
- The moderator will introduce the presenter at the beginning of each presentation.
- Then, the secretariat will start the presentation video. (In principle, you do not have to share your presentation by yourself.)
- After finishing the presentation, online viewers will send textual questions to the Q & A column, so please follow the moderator's instructions and answer those questions.
- The following environment is recommended.
  -Create the image resolution in XGA (1024 x 768).
  -Microsoft PowerPoint (2019) can be used as the application software.
  -The fonts that come standard with Microsoft PowerPoint, Times, Arial are recommended.

[Precautions]

- Do not post, modify, distribute or reproduce copyrighted material, trademarks, portrait rights or other property rights in any way without the prior written consent of the owners of these property rights.
- Regarding citations, please specify the source of the citation.
- Please exert caution regarding the protection of personal information such as name, age, surgery date, etc. This could lead to the identification of an individual.

Instruction for Chairs

The conference program will be presented as a hybrid style meeting.

- An invitation email that contains information about the login will be sent to the presenters/moderators through the Zoom system. The login URL will be included in the invitation email.
- At the real time webinar, the recorded lecture will be presented, and speakers/chairs are requested to join the discussion time. The presentation and Q & A session will be delivered live.
- After presentation, the discussion time (a question-and-answer session) will be held according to the moderator's instructions. The online viewer will send questions in the Q & A column. The onsite participants will ask questions using the microphone at the conference hall.
- After the conference, the recorded video will be posted on the on-demand presentation page.

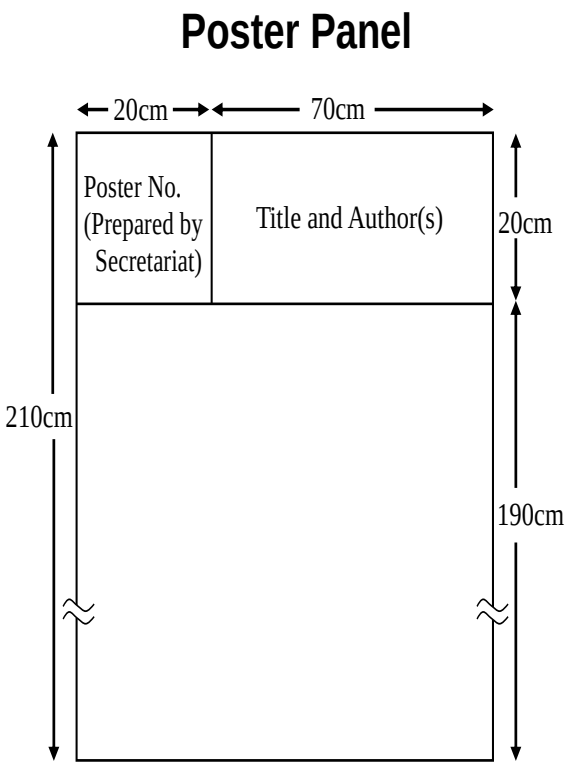
[For Chairs who will participate at the onsite conference venue]
Please be seated at the "next chair's seat" at least 10 minutes before the session will start. The seat will be located forward near the stage.

[For Chairs who will attend online]

- Please join Zoom at least 20 minutes before your session begins.
- Please turn on the microphone and the camera only when you are speaking. Please mute the microphone otherwise.
- Please introduce the presenter at the beginning of each presentation. Then, the secretariat will start the presentation video, or the speaker will start his/her presentation onsite.
- After finishing the presentation, please turn on the microphone and camera again. Online viewers will send textual questions to the Q&A column, and the onsite participants will ask questions using the microphone in the conference room. So please convey those questions and moderate the discussion.
- The following environment is recommended.
  -Create the image resolution in XGA (1024 x 768).
  -Microsoft PowerPoint (2019) can be used as the application software.
  -The fonts that come standard with Microsoft PowerPoint, Times, Arial are recommended.

Instruction for Onsite Poster Presentation

A panel width 90cm×length 210cm will be provided for each poster as the 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 located in the Room 2 (Sendai B) and Room 3 (Fuyou) 4th Floor, Hotel Metropolitan Sendai
Schedule of Onsite Poster is as follows.
Poster Attachment: 8:00-10:00 on Oct. 27
Poster Presentation: 16:50-18:00 on Oct. 27
Awarding Ceremony: 18:10-19:10 on Oct. 27
*Followed by Welcome Reception.
Poster Removal: after 13:30 on Oct. 28.
*For those who have not removed posters until above removal time, please accept that the secretariat will discard any posters that have remained.



Instruction for E-Poster Presentation

Please record your presentation (PowerPoint presentation with narration within 6 min.) in advance and submit the MP4 file (PowerPoint presentation with narration data converted to MP4) to the congress secretariat by uploading the data to the following uploading site.

Upload Site: https://midea-gd.net/ASfulSystem/index.php

Information for Poster Presentation is available at the following URL.
https://www.apasl-oncology2023.org/abs_presentation.html

If you have any questions, please contact the secretariat below.

Contact: APASL Oncology 2023 Sendai Congress Secretariat
c/o Academia Support Japan
Email: info@apasl-oncology2023.org
Tel: +81-3-6380-0102 Fax: +81-3-6380-0103
URL http://www.apasl-oncology2023.org

Awards

Excellent papers will be awarded as “Presidential Award”, “Investigator Award”, “Travel Award”.
Awarding Ceremony: The Awardees of Free Papers will be presented during 18:10-19:10 (Japan Standard Time) on October 27 (Friday).

Presidential Award

“APASL Oncology 2023 Sendai Presidential Award” will be awarded to whom performed the most excellent presentation in APASL Oncology 2023 Sendai to encourage to further their research and progress.

Investigator Award

The purpose of the “APASL Oncology 2023 Sendai 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 2023 Sendai Travel Award” will be awarded to whom performed the excellent presentation traveling to the onsite venue in APASL Oncology 2023 Sendai.

Contact

APASL Oncology 2023 Sendai Scientific Secretariat
Department of Gastroenterology,
Faculty of Medicine, Yamagata University, Japan

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1-24-7-920, Shinjuku, Shinjuku-ku, Tokyo, 160-0022 Japan
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Sponsors and Support Organization

The Organizing Committee of the APASL Oncology 2023 Sendai would like to express sincere gratitude to the following sponsors and organizations for supporting this conference.

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Sendai Tourism, Convention and International Association

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Program at a Glance Day 1: October 27 (Friday) 2023

	October 27 (Fryday)			
	Room 1	**Room 2**	**Room2, 3**	**Foyer**
8:00	7:30- Registration			
	8:30-8:40 **Opening Ceremony**			
9:00	8:40-9:10 **Opening Lecture** **Dr. Masao Omata**			
	9:10-10:10 **Workshop 1** **Systemic Chemotherapy & Oncology 1**	9:10-10:10 **Workshop 4** **Basic Science & Pathology 1**		
10:00				
	10:10-11:10 **Workshop 2** **Systemic Chemotherapy & Oncology 2**	10:10-11:10 **Workshop 5** **Basic Science & Pathology 2**		
11:00				
	11:20-11:40 **Keynote Lecture 1** **Dr. Grace L.H. Wong**		**Poster Viewing**	**Exhibition**
	11:40-12:00 **Keynote Lecture 2** **Dr. Gregory J. Gores**	11:40-12:00 **Keynote Lecture 4** **Dr. Man Fung Yuen**		
12:00	12:00-12:20 **President Lecture** **Dr. Yoshiyuki Ueno**			
	12:30-13:30 **Luncheon Seminar 1** (Eisai Co., Ltd. / MSD K.K.)	12:30-13:30 **Luncheon Seminar 2** (Chugai Pharmaceutical Co., Ltd.)		
13:00				
	13:40-14:10 **Special Lecture 1** **Dr. Shiv K. Sarin**			
14:00	14:10-14:40 **Special Lecture 2** **Dr. George K.K. Lau**			
	14:40-15:10 **Special Lecture 3** **Dr. Jia-Horng Kao**			
15:00				
	15:20-15:40 **Keynote Lecture 3** **Dr. Takahiro Kodama**	15:20-15:40 **Keynote Lecture 5** **Dr. Henry L.Y. Chan**		
16:00	15:40-16:40 **Workshop 3** **Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD**	15:40-16:40 **Workshop 6** **Basic Science & Pathology 3**		
17:00		16:50-18:00 **Onsite Poster Sessions** (Room 2 & Room 3)		
18:00	18:10-19:10 **Awarding Ceremony** 19:10-20:30 **Welcome Reception**			

*E-Posters are available at website https://www.apasl-oncology2023.org during the conference term.

Program at a Glance Day 2: October 28 (Saturday) 2023

	October 28 (Saturday)			
	Room 1	**Room 2**	**Room 2, 3**	**Foyer**
8:00				
	8:00-9:00 **Morning Seminar** (Gilead Sciences K.K.)			
9:00				
	9:10-10:10 **Workshop 7** **Systemic Chemotherapy & Oncology 3**	9:10-10:10 **Workshop 11** **Surgery & Transplantation**	**Poster Viewing**	**Exhibition**
10:00				
	10:20-11:20 **Workshop 8** **Systemic Chemotherapy & Oncology 4**	10:20-11:20 **Workshop 12** **Surgery & Transplantation, TACE, HAIC & Vascular Interventions**		
11:00				
	11:30-11:50 **Keynote Lecture 6** **Dr. Hayato Nakagawa**			
	11:50-12:10 **Keynote Lecture 7** **Dr. Mindie H. Nguyen**	11:50-12:10 **Keynote Lecture 8** **Dr. Tushar Patel**		
12:00				
	12:30-13:30 **Luncheon Seminar 3** (Gilead Sciences K.K. Medical Affairs)	12:30-13:30 **Luncheon Seminar 4** (AbbVie GK)		
13:00				
	13:40-14:25 **Special Lecture 4** **Dr. Masatoshi Kudo**			
14:00				
	14:35-15:35 **Workshop 9** **Hepatitis C, Hepatitis B**	14:35-15:47 **Workshop 13** **Tumor Markers & Biochemistry, CCC, Others**		
15:00				
	15:45-16:45 **Workshop 10** **Radiotherapy, Imaging & Diagnosis, irAE**			
16:00				
	16:45-17:00 **Closing Ceremony**			
17:00				

*E-Posters are available at website https://www.apasl-oncology2023.org during the conference term.

APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Scientific Program

Scientific Program

Day 1: October 27 (Friday) 2023

Room 1 (Sendai A)

8:30-8:40 Opening Ceremony

Opening Remarks: Dr. Yoshiyuki Ueno, President of APASL Oncology 2023 Sendai

8:40-9:10 Opening Lecture

Chair: Dr. Yoshiyuki Ueno (Japan)

Challenge of Oncology with or without Driver Genes; Liver, Lung and Pancreas

Dr. Masao Omata (Japan)

9:10-10:10 Workshop 1: Systemic Chemotherapy & Oncology 1

Chairs: Dr. Shiv K Sarin (India), Dr. Naoya Kato (Japan), Dr. Ken Shirabe (Japan) , Dr. Tatsuya Yamashita (Japan)

9:10-9:22 WS1-1

Multimodal Treatment Strategy with Atezolizumab plus Bevacizumab towards the Complete Response in Unresectable Hepatocellular Carcinoma

Dr. Haruhiko Takeda (Japan)

9:22-9:34 WS1-2

Late Line Treatment with Atezolizumab plus Bevacizumab Therapy is Less Effective in Unresectable Hepatocellular Carcinoma

Dr. Masashi Ninomiya (Japan)

9:34-9:46 WS1-3

Comparative Analysis of Atezolizumab plus Bevacizumab and Hepatic Artery Infusion Chemotherapy in Unresectable Hepatocellular Carcinoma: A Multi-center, Propensity Score Study

Dr. Pil Soo Sung (Korea)

9:46-9:58 WS1-4

Changes in Serum Growth Factors During Resistance to Ate-zolizumab Plus Bevacizumab Treatment in Patients with Un-resectable Hepatocellular Carcinoma

Dr. Goki Suda (Japan)

9:58-10:10 WS1-5

Predictive Factors for Durable Response in Patients Received Atezolizumab plus Bevacizumab Therapy for Unresectable Hepatocellular Carcinoma

Dr. Yutaka Yasui (Japan)

10:10-11:10 Workshop 2: Systemic Chemotherapy & Oncology 2

Chairs: Dr. Han-Chieh Lin (Taiwan), Dr. Masayuki Kurosaki (Japan), Dr. Hidekatsu Kuroda (Japan), Dr. Masafumi Ikeda (Japan)

10:10-10:22 WS2-1

A Prospective Study to Assess the Safety and Efficacy of Lenvatinib in Patients with Advanced Hepatocellular Carcinoma Aiming to Maximise Its Potential in Current Clinical Practice

Dr. Kazufumi Kobayashi (Japan)

10:22-10:34 WS2-2

Prognostic Factors for Survival in Patients with Intermediate-stage Unresectable Hepatocellular Carcinoma Treated with Lenvatinib or Atezolizumab plus Bevacizumab

Dr. Naoki Uchihara (Japan)

10:34-10:46 WS2-3

Immunokinetic Analysis Predicts Efficacy of Combination Immunotherapy for Advanced Hepatocellular Carcinoma

Dr. Takahiro Kodama (Japan)

10:46-10:58 WS2-4

Cabozantinib Therapy in Patients Previously Treated with Atezolizumab/Bevacizumab for Advanced Hepatocellular Carcinoma-Importance of Good Liver Function and Good Performance Status

Dr. Teiji Kuzuya (Japan)

10:58-11:10 WS2-5

Therapeutic Strategy for Advanced Hepatocellular Carcinoma with Combination of Systemic Therapy and Surgical Resection

Dr. Takahiro Nishio (Japan)

11:20-11:40 Keynote Lecture 1

Chair: Dr. Ryosuke Tateishi (Japan)

Strategies for Preventing NASH-derived HCC

Dr. Grace L.H. Wong (China)

11:40-12:00 Keynote Lecture 2

Chair: Dr. Naoya Sakamoto (Japan)

Cholangiocarcinoma: Seeking a Cure

Dr. Gregory J. Gores (USA)

12:00-12:20 President Lecture

Chair: Dr. Masao Omata (Japan)

In Search of Silver Bullet for HCC

Dr. Yoshiyuki Ueno (Japan)

12:30-13:30 Luncheon Seminar 1 (Sponsored by Eisai Co., Ltd. / MSD K.K.)

Chair: Dr. Naoya Kato (Japan)

The Value of Lenvatinib, Synthesized in Japan, in Patients with HCC-including Harmonization with Loco-regional Therapy

12:30-13:00 LS1-1

Positioning of Lenvatinib and Role of Adding Hepatic Arterial Infusion Chemotherapy to Lenvatinib for Unresectable Hepatocellular Carcinoma in Era of Immunotherapy

Dr. Takeshi Terashima (Japan)

13:00-13:30 LS1-2

New Treatment Strategies for Unresectable HCC ~The Positioning of Lenvatinib in Real-world Practice~

Dr. Kaoru Tsuchiya (Japan)

13:40-14:10 Special Lecture 1

Chair: Dr. Masao Omata (Japan)

Management of Portal Hypertension in Hepatocellular Carcinoma

Dr. Shiv K. Sarin (India)

14:10-14:40 Special Lecture 2

Chair: Dr. Osamu Yokosuka (Japan)

Systemic Therapy for Hepatocellular Carcinoma-2023 and Beyond

Dr. George K.K. Lau (China)

14:40-15:10 Special Lecture 3

Chair: Dr. Satoshi Mochida (Japan)

Development of HCC in HBV Patients

Dr. Jia-Horng Kao (Taiwan)

15:20-15:40 Keynote Lecture 3

Chair: Dr. Osamu Yokosuka (Japan)

Biomarker-based Precision Medicine in the Era of Combination Immunotherapy in HCC

Dr. Takahiro Kodama (Japan)

15:40-16:40 Workshop 3: Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD

Chairs: Dr. Yoichi Hiasa (Japan), Dr. Kenichi Ikejima (Japan), Dr. Shuji Terai (Japan)

15:40-15:52 WS3-1

The Difference of Branched-chain Amino Acids Tyrosine Ratio (BTR) among Chronic Liver Disease Comparing to Healthy Adult

Dr. Eiji Kakazu (Japan)

15:52-16:04 WS3-2

Agile 3+ and Agile 4, Non-invasive Tests for Liver Fibrosis, are Excellent Formulae to Predict Liver-related Events in Nonalcoholic Fatty Liver Disease

Dr. Kouichi Miura (Japan)

16:04-16:16 WS3-3

Impact of Liver Fibrosis Severity on Oncological Prognosis in Hepatocellular Carcinoma: 1-to-1 Individual Case-matched Analysis

Dr. Koya Yasukawa (Japan)

16:16-16:28 WS3-4

Impact of Chemotherapy on Liver

Dr. Harshita Dubey (India)

16:28-16:40 WS3-5

Big Data Analysis of Fatty Liver, Liver Stiffness and Liver Cancer Frequency within Cancer Center Hospitals

Dr. Hitoshi Mochizuki (Japan)

18:10-19:10 Awarding Ceremony

19:10-20:30 Welcome Reception

Day 1: October 27 (Saturday) 2023

Room 2 (Sendai B)

9:10-10:10 Workshop 4: Basic Science & Pathology 1

Chairs: Dr. Jin Mo Yang (Korea), Dr. Shinji Itoh (Japan), Dr. Naoshi Nishida (Japan), Dr. Akinobu Taketomi (Japan)

9:10-9:22 WS4-1

Immunoglobulin-like Transcript 2 as an Impaired Anti-tumor Cytotoxicity Marker of Natural Killer Cells in Patients with Hepatocellular Carcinoma

Dr. Sachiyo Yoshio (Japan)

9:22-9:34 WS4-2

Novel Monoclonal Antibody and ADAM17 Enzymatic Inhibitor could Induce NK Cell-mediated Cytotoxicity in HCC by Targeting NKG2D Ligands

Dr. Jun Arai (Japan)

9:34-9:46 WS4-3

Fibroblast Growth Factor Inhibition by Molecular-targeted Agents Mitigates Immuno-suppressive Tissue Microenvironment in Hepatocellular Carcinoma

Dr. Hiroyuki Suzuki (Japan)

9:46-9:58 WS4-4

Prevention of Liver Carcinogenesis by Glycine in Hepatocyte-specific PTEN Knockout Mice

Dr. Kazuyoshi Kon (Japan)

9:58-10:10 WS4-5

Role of ZHX Family Proteins in Hepatocarcinogenesis Studied by Immunohistochemical Staining

Dr. Yuhong Ma (Japan)

10:10-11:10 Workshop 5: Basic Science & Pathology 2

Chairs: Dr. Lai Wei (China), Dr. Hayato Hikita (Japan), Dr. Hironori Koga (Japan), Dr. Masashi Ninomiya (Japan)

10:10-10:22 WS5-1

Intrahepatic IgA Complex Induces Polarization of Cancer Associated Fibroblasts into the Matrix Phenotype in the Tumor Microenvironment of HCC

Dr. Pil Soo Sung (Korea)

10:22-10:34 WS5-2

The Role and Mechanism of LincRNA Encoded Peptide in the Progression of Hepatocellular Carcinoma

Dr. Guang-Zhi Jin (China)

10:34-10:46 WS5-3

Interaction between HSC and LSEC Populations in the Premalignant Environment of DEN-treated Cytoglobin Knock-out Mice

Dr. Ha T. Nguyen (Japan)

10:46-10:58 WS5-4

Anti-proliferative Effects of a Flavonoid from Anomianthus Dulcis Sincl. on Hepatocellular Carcinoma

Dr. Charupong Saengboonmee (Thailand)

10:58-11:10 WS5-5

Protective Effect of Ischemic Preconditioning on Hepatic Ischemia-reperfusion Injury in Rats

Dr. Naoki Hashimoto (Japan)

11:40-12:00 Keynote Lecture 4

Chair: Dr. Nobuyuki Enomoto (Japan)

Strategies for Terminating HBV related HCC

Dr. Man-Fung Yuen (China)

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

Chair: Dr. Tatsuya Yamashita (Japan)

Unlocking the Potential of Combination Immunotherapy in Advanced Hepatocellular Carcinoma

Dr. Sadahisa Ogasawara (Japan)

15:20-15:40 Keynote Lecture 5

Chair:Dr. Jun Inoue (Japan)

Deciphering HCC Risk Scores for Chronic Hepatitis B

Dr. Henry L.Y. Chan (China)

15:40-16:40 Workshop 6: Basic Science & Pathology 3

Chairs: Dr. Jose Sollano (Philippines), Dr. Takahiro Kodama (Japan),
Dr. Sadahisa Ogasawara (Japan), Dr. Masahito Shimizu (Japan)

15:40-15:52 WS6-1

Enhancing Tumor Immunogenicity of Hepatocellular Carcinoma using a Novel Cancer Vaccine

Dr. Masao Nakajima (Japan)

15:52-16:04 WS6-2

High-grade Nuclear Atypia is an Unfavorable Factor for Postoperative Recurrence of Hepatocellular Carcinoma

Dr. Shinji Mizuochi (Japan)

16:04-16:16 WS6-3

Findings of Liver Pathology in Autopsy

Dr. Amar Ranjan (India)

16:16-16:28 WS6-4

Significance of Partial Portal Arterialization in Small Bowel Transplantation for the Liver

Dr. Naoki Hashimoto (Japan)

Day 2: October 28 (Saturday) 2023

Room 1 (Sendai A)

8:00-9:00 Morning Seminar 1 (Sponsored by Gilead Sciences K.K.)

Chair: Dr. Hidekatsu Kuroda (Japan)

A New Era in Liver Diseases: Recent Advances and Issues in Hepatitis C Virus Infection and Liver Cancer

Dr. Jun Inoue (Japan)

9:10-10:10 Workshop 7: Systemic Chemotherapy & Oncology 3

Chairs: Dr. Tawesak Tanwandee (Thailand), Dr. Yosuke Nakai (Japan), Dr. Motoyuki Otsuka (Japan), Dr. Kaoru Tsuchiya (Japan)

9:10-9:22 WS7-1

A Prospective Study to Assess the Safety and Efficacy of Ramucirumab in Advanced Hepatocellular Carcinoma Patients in Japanese Real-world Practice: R-evolution Study

Dr. Kazufumi Kobayashi (Japan)

9:22-9:34 WS7-2

A Randomized Phase II Trial to Assess Safety and Efficacy of Regorafenib in Patients with Advanced Hepatocellular Carcinoma who were not Included in the RESORCE Trial: REGAIN Trial

Dr. Keisuke Koroki (Japan)

9:34-9:46 WS7-3

Efficacy of Lenvatinib Combined with Transcatheter Intraarterial Therapies for Patients with Advanced-stage of Hepatocellular Carcinoma: A Propensity Score Matching

Dr. Shigeo Shimose (Japan)

9:46-9:58 WS7-4

The Effectiveness of Durvalumab plus Tremelimumab Treatment for Hepatocellular Carcinoma after Treatment with Anti-VEGF Drugs

Dr. Takayoshi Oikawa (Japan)

9:58-10:10 WS7-5

Early Experience of Durvalumab plus Tremelimumab in Patients with Unresectable Hepatocellular Carcinoma

Dr. Kaoru Tsuchiya (Japan)

10:20-11:20 Workshop 8: Systemic Chemotherapy & Oncology 4

Chairs: Dr. Ji-Dong Jia (China), Dr. Atsushi Hiraoka (Japan), Dr. Taro Takami (Japan), Dr. Kazuomi Ueshima (Japan)

10:20-10:32 WS8-1

Survival Improvements in Advanced Hepatocellular Carcinoma with Systemic Therapy Over the Past Decade

Dr. Ryo Yano (Japan)

10:32-10:44 WS8-2

Association between Presarcopenia and Clinical Outcomes in Patients with Advanced Hepatocellular Carcinoma Undergoing Systemic Therapy: A Comprehensive Study and Meta-Analysis

Dr. Ching-Sheng Hsu (Taiwan)

10:44-10:56 WS8-3

Consistent Efficacy of Hepatic Artery Infusion Chemotherapy Irrespective of PD-L1 Positivity in Unresectable Hepatocellular Carcinoma

Dr. Pil Soo Sung (Korea)

10:56-11:08 WS8-4

Genetic Discrimination between MC and IM could be Useful in Planning Tumor-specific Treatment Strategies for Recurrent Hepatocellular Carcinoma

Dr. Yuji Iimuro (Japan)

11:08-11:20 WS8-5

Abdominal Pain Accompanied by Elevated Serum Inflammatory Markers and Biliary Enzymes for Diagnosing Immune Checkpoint Inhibitor-induced Sclerosing Cholangitis

Dr. Takanori Ito (Japan)

11:30-11:50 Keynote Lecture 6

Chair: Dr. Naoya Kato (Japan)

Molecular Mechanisms and Cellular Origins of Biliary Tract Cancer: Cutting-edge Knowledge from Mouse Models

Dr. Hayato Nakagawa (Japan)

11:50-12:10 Keynote Lecture 7

Chair: Dr. Yasuhito Tanaka (Japan)

Strategies for Terminating HCV-related HCC

Dr. Mindie H. Nguyen (USA)

12:30-13:30 Luncheon Seminar 3 (Sponsored by Gilead Sciences K.K. Medical Affairs)

Chair: Dr. Motoyuki Otsuka (Japan)

Recent Topics about Hepatocellular Carcinoma: Focusing on Risks of Hepatitis and Advances in the Therapy

Dr. Masayuki Kurosaki (Japan)

13:40-14:25 Special Lecture 4

Chair: Dr. Tetsuo Takehara (Japan)

All Stages of HCC Patients Benefit from Systemic Therapy Combined with Locoregional Therapy

Dr. Masatoshi Kudo (Japan)

14:35-15:35 Workshop 9: Hepatitis C, Hepatitis B

Chairs: Dr. Barjesh C. Sharma (India), Dr. Hirayuki Enomoto (Japan), Dr. Tatsuya Kanto (Japan)

14:35-14:47 WS9-1

Usefulness of FIB-4 Index and ALT at 1 Year of Nucleos(t)ide Analog Treatment for Prediction of Hepatocellular Carcinoma in Chronic Hepatitis B Patients

Dr. Jun Inoue (Japan)

14:47-14:59 WS9-2

MxB Induced in Mitochondria by IFN Inhibits HBV Replication by Activating the RIG-I Signaling Pathway

Dr. Masazumi Onuki (Japan)

14:59-15:11 WS9-3

HCV Clearance Improves Amino Acids Imbalance in Patients with Hepatitis C Regardless of the Presence of Advanced Fibrosis or Previous Treatment of HCC

Dr. Masaaki Mino (Japan)

15:11-15:23 WS9-4

Clinical and Imaging Features of Hypervascular De Novo Hepatocellular Carcinoma after HCV Eradication

Dr. Tomoko Tanaka (Japan)

15:23-15:35 WS9-5

Recurrence and Prognosis of Patients with Primary Hepatocellular Carcinoma Treated with Radiofrequency Ablation

Dr. Rie Goka (Japan)

15:45-16:45 Workshop 10: Radiotherapy, Imaging & Diagnosis, irAE

Chairs: Dr. A Kadir Dokmeci (Turkey), Dr. Teiji Kuzuya (Japan) , Dr. Shuuichiro Shiina (Japan), Dr. Ryosuke Tateishi (Japan)

15:45-15:57 WS10-1

Effectiveness of Repeated Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma

Dr. Tomokazu Kawaoka (Japan)

15:57-16:09 WS10-2

Establishment of Hepatic Tumor Differentiation and Hepatocellular Carcinoma Grading Method by Quantitative Analysis of Contrast-enhanced Ultrasound Images Using Microbubbles

Dr. Tamami Abe (Japan)

16:09-16:21 WS10-3

Differentiation of AST/ALT Elevation during Immunotherapy in Patients with Advanced Hepatocellular Carcinoma and Other Cancers

Dr. Ryo Izai (Japan)

16:21-16:33 WS10-4

The Current Status of IMH in Our Hospital and Experience with the Use of Tacrolimus in Cases Resistant to PSL and MMF

Dr. Mio Tsuruoka (Japan)

16:33-16:45 WS10-5

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

Dr. Shuichiro Shiina (Japan)

16:45-17:00 Closing Ceremony

Closing Remarks: Dr. Yoshiyuki Ueno, President of APASL Oncology 2023 Sendai

Day 2: October 28 (Saturday) 2023

Room 2 (Sendai B)

9:10-10:10 Workshop 11: Surgery & Transplantation

Chairs: Dr. Rino Gani (Indonesia), Dr. Nobuhisa Akamatsu (Japan),
Dr. Kiyoshi Hasegawa (Japan), Dr. Takayoshi Oikawa (Japan)

9:10-9:22 WS11-1
Withdrawed

9:22-9:34 WS11-2

Difficulty in Survival Prediction for Hepatocellular Carcinoma and Cholangicarcinoma after Orthotopic Liver Transplantation

Dr. Akinobu Takaki (Japan)

9:34-9:46 WS11-3

Strategy of Living Donor Liver Transplantation for Unresectable Perihilar Cholangiocarcinoma

Dr. Takashi Ito (Japan)

9:46-9:58 WS11-4

Strategy for Liver Transplantation with Marginal Donor for HCC Cases

Dr. Kazuaki Tokodai (Japan)

9:58-10:10 WS11-5

Laparoscopic Left Medial Sectionectomy According to Tumor Localization

Dr. Yukio Tokumitsu (Japan)

10:20-11:20 Workshop 12: Surgery & Transplantation, TACE, HAIC & Vascular Interventions

Chairs: Dr. Michiie Sakamoto (Japan), Dr. Shinji Tanaka (Japan),
Dr. Michiaki Unno (Japan)

10:20-10:32 WS12-1

The Impact of Local Ablation in Resected Hepatocellular Carcinoma

Dr. Yusuke Nishi (Japan)

10:32-10:44 WS12-2

Ferroptosis is Induced by Lenvatinib through Fibroblast Growth Factor Receptor-4 Inhibition and Play a Key Role in the Suppression of Hepatocellular Carcinoma

Dr. Norifumi Iseda (Japan)

10:44-10:56 WS12-3

Hyperamylasemia after Hepatic Resection

Dr. Naoki Hashimoto (Japan)

10:56-11:08 WS12-4

The Effectiveness of the Locoregional Treatment Using Hepatic Arterial Infusion Chemotherapy New FP for Locally Progressed Hepatocellular Carcinoma

Dr. Hideki Iwamoto (Japan)

11:08-11:20 WS12-5

Effect of Distal Splenorenal Shunt plus Splenopancreatic Disconnection on Glucose and Amino Acid Metabolism

Dr. Naoki Hashimoto (Japan)

11:50-12:10 Keynote Lecture 8

Chair: Dr. Hiroyuki Isayama (Japan)

RNA Therapeutics for Liver Cancers

Dr. Tushar Patel (USA)

12:30-13:30 Luncheon Seminar 4 (Sponsored by AbbVie GK)

Chair: Dr. Naoya Sakamoto (Japan)

Multidisciplinary Treatment Including DEB-TACE Combined with HAIC and iCIs should be Considered to Control HCC ～Including Patients after DAA Treatment～

Dr. Yasuteru Kondo (Japan)

14:35-15:47 Workshop 13: Tumor Markers & Biochemistry, CCC, Others

Chairs: Dr. Cosmas A. Lesmana (Indonesia), Dr. Tatsuo Kanda (Japan), Dr. Tsutomu Masaki (Japan), Dr. Kazuhiro Nouso (Japan)

14:35-14:47 WS13-1

Diagnostic Value of Serum GPC3 in Early Stage of HCC

Dr. Munkhbayar Semchin (Mongolia)

14:47-14:59 WS13-2

Metabolic Profiling Identifies Key Metabolic Biochemical Pathways Associated with Recurrence of Hepatocellular Carcinoma

Dr. Hongping Xia (Singapore)

14:59-15:11 WS13-3

The Bile Level of Cytokeratin 7 as a Diagnostic Marker for Cholangiocarcinoma

Dr. Alzhraa Alkhatib (Egypt)

15:11-15:23 WS13-4

Withdrawed

15:23-15:35 WS13-5

Efficacy of NewFP Therapy for Unresectable Advanced Intrahepatic Cholangiocarcinoma

Dr. Hiroto Ota (Japan)

15:35-15:47 WS13-6

Support and Implementation system for Clinical Cancer Research at the Prefectural Designated Regional Cancer Centers and Hospital

Dr. Kenji Amemiya (Japan)

Onsite Poster Sessions

Day 1: October 27 (Friday) 2023

Room 2 (Sendai B) & Room 3 (Fuyo) 16:50-18:00

Onsite Poster Session 1: "Systemic Chemotherapy & Oncology 1"

Chair: Dr. Kiyoaki Ito (Japan)

16:50-17:20

P1-1 10069

Characteristic of HCC Patients Achieving Clinical Complete Response Treated with Atezolizumab plus Bevacizumab

Dr. Issei Saeki (Japan)

P1-2 10057

Usefulness of IL-6 as a Therapeutic Response Predictor in Atezolizumab + Bevacizumab Combination Therapy for Hepatocellular Carcinoma

Dr. Takanori Mukozu (Japan)

P1-3 10076

Atezolizumab + Bevacizumab Post-Treatment Strategies and Outcomes

Dr. Shuntaro Obi (Japan)

P1-4 10027

Treatment Outcomes of ABC Conversion Therapy at Our Hospital

Dr. Akihiro Deguchi (Japan)

P1-5 10005

Clinical Features of Proteinuria During Atezolizumab plus Bevacizumab Treatment

Dr. Fujimasa Tada (Japan)

17:20-17:50

Onsite Poster Session 2: "Systemic Chemotherapy & Oncology 2"

Chair: Dr. Kazumichi Abe (Japan)

P2-1 10030

Therapeutic Efficacy of Conversion Therapy after Systemic Chemotherapy for Patients with Unresectable Hepatocellular Carcinoma

Dr. Takashi Tanaka (Japan)

P2-2　10053

The Impact of Bevacizumab Withdrawal on Prognosis in Atezolizumab + Bevacizumab Combination Therapy for Unresectable Hepatocellular Carcinoma

Dr. Kei Amioka (Japan)

P2-3　10107

Clinical Factors Associated with the Therapeutic Efficacy of Atezolizumab plus Bevacizumab in Patients with Unresectable Hepatocellular Carcinoma: A Multicenter Prospective Observational Study

Dr. Kazuki Maesaka (Japan)

P2-4　10098

Proangiogenic Cytokines are Useful Prognostic Markers for the Advanced Hepatocellular Carcinoma Patients with Atezolizumab plus Bevacizumab Treatment

Dr. Takuya Adachi (Japan)

P2-5　10050

Role of Prognostic Nutritional Index in Predicting Survival during Atezolizumab plus Bevacizumab Treatment in Unresectable Hepatocellular Carcinoma: A Multicenter Study in Tohoku, Japan

Dr. Masashi Fujita (Japan)

16:50-17:20

Onsite Poster Session 3: “Systemic Chemotherapy & Oncology 3”

Chair: Dr. Jun Itakura (Japan)

P3-1　10148

Immune-related Adverse Event Occurrence and Treatment Response to Immune Checkpoint Inhibitors in Patients with Gastrointestinal Cancer; Using All Organ Cancers as the Denominator

Dr. Kaori Matsumoto (Japan)

P3-2　10080

Serum Aldolase Predicts Dose Reduction or Interruption of Cabozantinib in Patients with Hepatocellular Carcinoma

Dr. Hironao Okubo (Japan)

P3-3 10142

The Safety and Efficacy of Combination Immunotherapy of TACE (Transarterial-chemoembolization) and Autologous Natural Killer Cells in Patients with Hepatocellular Carcinoma

Dr. Jooho Lee (Korea)

P3-4 10071

Impact of Grip Strength in Patients with Unresectable Hepatocellular Carcinoma Treated with Atezolizumab plus Bevacizumab

Dr. Kei Endo (Japan)

P3-5 10058

Effect of Atezolizumab plus Bevacizumab Combination Therapy on Skeletal Muscle Mass and Cardiac Function by Age in Patients with Hepatocellular Carcinoma

Dr.Hideki Nagumo (Japan)

17:20-17:44

Onsite Poster Session 4: "TACE, HAIC, Imaging, Radiation"

Chair: Dr. Kouichi Miura (Japan)

P4-1 10088

Indications for Arterial Infusion Chemotherapy from the Atezolizumab + Bevacizumab (ATZ+BEV) GTO Cohort- HAIC is Always the Last Line of Defense-

Dr. Shuntaro Obi (Japan)

P4-2 10075

Long-term Prognosis of Stereotactic Body Radiotherapy Versus Radiofrequency Ablation in Patients with Small Hepatocellular Carcinoma Evaluated by Hepatic Reserve, Single-center Study

Dr. Yasuhide Motoyoshi (Japan)

P4-3 10106

Comparison of Diagnostic Accuracy between Fibroscan 630 and MR Elastography for Diagnosing Esophagogastric Varices by Measuring Splenic Stiffness

Dr. Kento Imajo (Japan)

P4-4 10102

The Diagnostic Ability for Microvascular Invasion Using Contrast Enhanced Ultrasopnography

Dr. Takashi Nishimura (Japan)

16:50-17:14

Onsite Poster Session 5: "Basic Science & Pathology 1"

Chair: Dr. Masatoshi Ishigami (Japan)

P5-1 10044

Clinicopathological Characteristics and Molecular Analysis of Lymphocyte-rich HCC

Dr. Kana Tsutsui (Japan)

P5-2 10101

Identification of the Possible Target Genes of Hepatoma-derived Growth Factor in Hepatoma Cells

Dr. Hirayuki Enomoto (Japan)

P5-3 10085

Differential Diagnosis of Intrahepatic Metastasis (IM) and Multicentric Carcinogenesis (MC) - How Close can Clinical Indicators Get to the Genome?

Dr. Shuntaro Obi (Japan)

P5-4 10087

Differential Diagnosis of IM and MC by Comprehensive Genomic Profiling (CGP) Changes Treatment Strategies

Dr. Shuntaro Obi (Japan)

17:14-17:38

Onsite Poster Session 6: "Basic Science & Pathology 2"

Chair: Dr. Satoru Joshita (Japan)

P6-1 10081

High-fat Diet Promotes Hepatic Fibrosis and Tumorigenesis in a Rat Cirrhosis Model

Dr. Daisuke Taguchi (Japan)

P6-2 10049

Dual Angiotensin II Receptor and Neprilysin Inhibitor Attenuates Liver Fibrosis by Preventing Hepatic Stellate Cell Activation

Dr. Junya Suzuki (Japan)

P6-3 10018

A Novel Hepatitis Delta Virus (HDV) in Vitro Carcinogenesis Model

Dr. Shinya Sato (Japan)

P6-4 10065

Impact of TIGAR on Malignant Activity and Resistance to Ferroptosis in Intrahepatic Cholangiocarcinoma

Dr. Katsuya Toshida (Japan)

16:50-17:14

Onsite Poster Session 7: "Basic Science & Pathology 3"

Chair: Dr. Kazuyoshi Kon (Japan)

P7-1 10054

Investigation of the Association between Receptor Type Tyrosine Kinase Expression and Genetic Variation Using TCGA HCC Data

Dr. Yoshinari Asaoka (Japan)

P7-2 10014

Glucagon-like Peptide-1 Receptor Agonist, Semaglutide Attenuates Chronic Liver Disease-induced Skeletal Muscle Atrophy in Diabetic Mice

Dr. Satoshi Iwai (Japan)

P7-3 10061

In Vitro and in Vivo Antitumor Effect of Biofabricated Silver Nanoparticles of Caffeic Acid against Hepatocarcinogenesis by Upregulation of Bax/Bcl2

Dr. Ekta Yadav (India)

P7-4 10060

Development and Assessment of a Novel Self Nano Emulsifying Formulation of Furosemide: A Drug Employed in Treating Portal Hypertension

Dr. Pankajkumar Yadav (India)

17:14-17:38

Onsite Poster Session 8: "Tumor Markers & Biochemistry"

Chair: Dr. Takumi Kawaguchi (Japan)

P8-1 10024

Clinical Usefulness of Tumor Markers AFP, L3, and DCP for Treatment of Hepatocellular Carcinoma

Dr. Yoshiko Fukunishi (Japan)

P8-2 10052

Evaluation of Glypican-3 Protein in the Tissues of Hepatocellular Carcinoma by Tissue Microarray

Dr. Batchimeg Batbaatar (Mongolia)

P8-3 10066

Diagnostic Marker of Mitochondrial Dysfunction, AREG, is Associated with Tumor Size in Hepatocellular Carcinoma

Dr. Katsuya Nagaoka (Japan)

P8-4 10002

Andrographolides Regulate c-Myc Stability and Demonstrate Cytotoxic and Genotoxic Activity in CD133+ Multi-drug Resistant Hepatocellular Carcinoma Cells via Small Molecule 20S Proteasome Activation

Dr. Glenn Oyong (Philippines)

16:50-17:20

Onsite Poster Session 9: "Surgery & Transplantation"

Chair: Dr. Yuji Iimuro (Japan)

P9-1 10035

Prognosis of the Patients with Multiple Hepatocellular Carcinoma who Underwent Initial Liver Resection

Dr. Hidetake Amemiya (Japan)

P9-2 10113

Impact of Justifying MELD Score Exception by MELD-ALBI Selection on the Outcome of HCC Transplantation

Dr. Alzhraa Alkhatib (Egypt)

P9-3 10092

Usefulness of Laparoscopic Liver Resection for Patients with Ruptured Hepatocellular Carcinoma

Dr. Masayasu Aikawa (Japan)

P9-4 10036

Influence of Child-Pugh B7 and B8/9 Cirrhosis on Laparoscopic Liver Resection for Hepatocellular Carcinoma: A Retrospective Cohort Study

Dr. Yukihiro Watanabe (Japan)

P9-5 10146

Efficacy and Safeness of Polyglycolic Acid Felt with Fibrin Glue at the Liver Cut Surface for Prevention of Postoperative Bile Leakage in Laparoscopic Liver Resection

Dr. Kenichiro Takase (Japan)

17:20-17:44

Onsite Poster Session 10: "Liver Cirrhosis & Sarcopenia"

Chair: Dr. Sachiyo Yoshio (Japan)

P10-1 10037

VWF/ADAMTS13 Ratio as a Potential Predictive Biomarker for Acute Kidney Injury Onset in Cirrhosis

Dr. Shohei Asada (Japan)

P10-2 10040

Diagnostic Markers for Portal Vein Thrombosis in Patients with Cirrhosis PVT

Dr. Tadashi Namisaki (Japan)

P10-3 10004

The Geriatric Nutritional Risk Index is a Useful Predictor of Muscle Volume Loss Regardless of Gender

Dr. Atsushi Hiraoka (Japan)

P10-4 10131

Coexistence of Muscle Atrophy and High Subcutaneous Adipose Tissue Predicts Poor Prognosis in Hepatocellular Carcinoma

Dr. Masatsugu Ohara (Japan)

16:50-17:14

Onsite Poster Session 11: "Hepatitis C, Hepatitis B"

Chair: Dr. Tadashi Namisaki (Japan)

P11-1 10103

High HBV DNA Level Increase the Risk of Tumor Recurrence after Surgical Resection or Ablative Therapy in Patients with HBV related Hepatocellular Carcinoma

Dr. Ji Hoon Kim (Korea)

P11-2 10020

Four-year Safety and Effectiveness of Tenofovir Alafenamide in Treatment-experienced Patients with Chronic Hepatitis B

Dr. Eiichi Ogawa (Japan)

P11-3 10123

The Genotypic Association of Hepatitis C Associated Oral Lichen Planus and Its Rsponse to Direct Acting Antivirals- A Case Series

Dr. Dexton Johns (India)

P11-4 10034

Directly Acting Antivirals Improve Insulin Resistance in Non-diabetic Patients with Hepatitis C: A Meta-analysis

Dr. P.Lamichhane (Nepal)

17:14-17:38

Onsite Poster Session 12: "Hepatitis C"

Chair: Dr. Atsushi Tanaka (Japan)

P12-1 10095

A Novel Formula Used for Predicting Hepatocellular Carcinoma after the Achievement of SVR by DAAs in Patients with Chronic Hepatitis C

Dr. Hiroki Ono (Japan)

P12-2 10074

Hepatic Steatosis is a Risk Factor for All-organ Carcinogenesis in Post-SVR Patients

Dr. Shuntaro Obi (Japan)

P12-3 10082

Surveillance should Continue after SVR-Carcinogenesis Continues to Increase in a Linear Fashion-

Dr. Shuntaro Obi (Japan)

P12-4 10084

Continued Surveillance after SVR Yields a Prognosis Equivalent to the Standardized Mortality Ratio (SMR)

Dr. Shuntaro Obi (Japan)

16:50-17:14

Onsite Poster Session 13: "NASH/ NAFLD & Genetic/ Metabolic Disease"

Chair: Dr. Eiji Kakazu (Japan)

P13-1 10039

Favorable Liver and Skeletal Muscle Changes in Patients with NAFLD and Type 2 Diabetes Receiving GLP-1 Receptor Agonist

Dr. Takuya Wada (Japan)

P13-2 10043

Effects of SGLT2 Inhibitors on Liver Steatosis and Fibrosis in Non-alcoholic Fatty Liver Disease and Type 2 Diabetes: A Meta-analysis

Dr. A. Agrawal (Nepal)

P13-3 10079

Effects of Lanifibranor on High-Fat Diet-Induced-Nonalcoholic Fatty Liver Disease and Associated Mood Disorder in Mice

Dr. Fang Yu Hsu (Taiwan)

P13-4 10025

Vitamin D Deficiency Exacerbates Alcohol-related Liver Injury via Gut Barrier Disruptionand Hepatic Overload of Endotoxin

Dr. Akihiko Shibamoto (Japan)

17:14-17:32

Onsite Poster Session 14: "Others 1"

Chair: Dr. Keisuke Kakizaka (Japan)

P14-1 10047

Clinical Features Related to the Prognosis of Patients with Ruptured Hepatocellular Carcinoma as Initial Symptom

Dr. Emi Yanagihara (Japan)

P14-2 10070

The Clinical Results of Switching from Zoledronic Acid Hydrate to Denosumab for Bone Metastasis of Hepatocellular Carcinoma, Single-center Simple Open-labeled Prospective Interventional Trial

Dr. Kensuke Naruto (Japan)

P14-3 10122

Health Related Quality of Life of Hepatocellular Carcinoma Metastasis to Oral Cavity -A Systematic Review

Dr. Dexton Johns (India)

16:50-17:14

Onsite Poster Session 15: "Others 2"

Chair: Dr. Masafumi Fujita (Japan)

P15-1 10055

Long-Term Outcomes and Incidence of Hepatocellular Carcinoma in Primary Biliary Cholangitis Complicated with CREST Syndrome

Dr. Kazumichi Abe (Japan)

P15-2 10007

Prediction of Recurrence after Curative Treatment for Hepatocellular Carcinoma Using aMAP Risk Score

Dr. Hideko Ohama (Japan)

P15-3 10133

Journey and Evolution of Comprehensive Genomic Analysis: Integrating Panel Sequencing to Expert Panel Implementation

Dr. Yosuke Hirotsu (Japan)

P15-4 10013

Experience of Comprehensive Cancer Genome Profiling Test in Intrahepatic Cholangiocarcinoma in Our Institution

Dr. Hiroyuki Okuyama (Japan)

E-Posters

E-Posters (Case Reports)

*E-Posters are available to view through APASL Oncology 2023 Sendai website.
https://www.apasl-oncology2023.org/index.html

E-1 10001

A Case of Hepatocellular Carcinoma Associated with Glycogen Storage Disease Type Ib

Dr. Shingo Satou (Japan)

E-2 10008

A Case of Large Hepatic Hemangioma with Extrahepatic Growth and Indicated for Resection

Dr. Keita Shirahata (Japan)

E-3 10011

Primary Hepatic Methotrexate-associated Lymphoproliferative Disorders 5 Months after Methotrexate Administration

Dr. Yasuki Hatayama (Japan)

E-4 10019

Hepatocellular Carcinoma & Hepatic Cystic Echinococcosis Presenting as Synchronous Single Lesion

Dr. Dipankar Das (India)

E-5 10021

A Case of Hepatocellular Carcinoma with Lung Metastasis that has been Controlled for more than 1 Year with Cabozantinib Introduced as the Fifth Line of Therapy

Dr. Rintaro Kobayashi (Japan)

E-6 10048

Atezolizumab plus Bevacizumab Enable to Perform Conversion Surgery for a Lymph Node Metastasis of Hepatocellular Carcinoma

Dr. Ken Sato (Japan)

E-7 10077

Chameleon Sign in CT Images of Breast Cancer Liver Metastases

Dr. Shuntaro Obi (Japan)

E-8 10078

Clinical Study of Hepatocellular Carcinoma with Bone Metastasis Treated with Palliative Radiotherapy

Dr. Kyoko Hoshikawa (Japan)

E-9 10089

A Case of Bile Duct Stenosis after Percutaneous Ablation Therapy that was Successfully Treated with Drainage

Dr. Shuntaro Obi (Japan)

E-10 10090

Successful Response to Immune Checkpoint Inhibitor Therapy after Radiation Treatment in a Case of Stage IVb Hepatocellular Carcinoma

Dr. Yamato Nagata (Japan)

E-11 10091

A Case of Post-RFA Hemothorax Improved with IVR and Intrathoracic Hematoma Removal

Dr. Keita Maki (Japan)

E-12 10094

A Case of Remission of Advanced Hepatocellular Carcinoma with Vascular Invasion Treated with Radiation and Sorafenib Combination Therapy

Dr. Tomohiro Katsumi (Japan)

E-13 10124

The Value of Ultrasound in Diagnosing Coexisting Primary Liver Tumor and Renal Amyloidosis in a Patient with COPD: A Case Report

Dr. Rostyslav Bubnov (Ukraine)

E-14 10125

Not the Usual: Diagnostic Dilemma in a Large Well Differentiated, Non- AFP Producing Hepatocellular Carcinoma with Atypical Features on Non-Invasive Imaging

Dr. Christine P. Velasquez (Philippines)

E-15 10126

A Case of Hepatocellular Carcinoma Associated with Hepatic Sarcoidosis

Dr. Fumiya Suzuki (Japan)

E-16 10138

Successful Treatment of Hepatocellular Carcinoma by Radiofrequency Ablation with Indocyanine Green Fluorescence Laparoscopy

Dr. Yosuke Otsuka (Japan)

E-17 10143

Imaging Insights into the Diagnosis and Management of Gallbladder Lesions in a High-Risk Patient: A Case Report

Dr. Rostyslav Bubnov (Ukraine)

E-18 10144

Case Report: Coexisting Liver-Gallbladder Oncology with Calculous Inflammation and Cholestasis - A Comprehensive Ultrasonographic Evaluation

Dr. Rostyslav Bubnov (Ukraine)

APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Abstracts

Lectures

Opening Lecture

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

Challenge of Oncology with or without Driver Genes; Liver, Lung and Pancreas

For the last 14 years, I worked at hospitals dealing with 30,000 patients suffering from different types of cancers. We established GAC (Genome Analysis Center) which dealt with more than 3,000 samples for genome analysis. These include lung, obstetric gynecology, urological, gastrointestinal and hepatobiliary cancers. It is becoming so clear that the neoplasm with or without targetable driver genes may have different treatment outcomes. Therefore, development of new oncological drugs, especially stage Ⅲ and Stage Ⅳ may be so different in different fields. The liver cancer does not have pivotal or representative driver genes, therefore, it might be the greatest challenge for us to tackle with the solid tumors without obvious “drivers”.

President Lecture

Dr. Yoshiyuki Ueno
Professor and Chairman
Department of Gastroenterology,
Faculty of Medicine, Yamagata University
Japan

In Search of Silver Bullet for HCC

Hepatocellular carcinoma (HCC) has been a great threat to human health regardless of geographical distribution. Although remarkable breakthrough has been made in the past several decades for prevention and treatment of viral hepatitis, still HCC is increasing its risk. Actually, 905,700 people were diagnosed with and 830,200 people died from liver cancer in 2020. Moreover, the number of new cases and deaths from liver cancer could rise by >55% by 2040. Thus, HCC remains to be global risk for next decades. Of course, we have combated for this disease with every available means, such as surgery, loco-regional therapy, IVR, drug therapy and radiotherapy. Introduction of molecular targeting drug has been a landmark for the treatment of HCC. The following TKIs have been contributing for improving patients care, however the ‘cure’ is hard to achieve only with this treatment option. The next breakthrough was cancer immunotherapy. With this treatment, certain proportion of patients achieved complete response. However, still majority of patients still need to struggle in treatment cascade. Thus, we are still in the middle of in search of silver bullet for the treatment of HCC. In this session, current therapeutic strategy will be summarized along with future perspective.

Special Lecture 1

Dr. Shiv K. Sarin

Senior Professor, Department of Hepatology,

Chancellor,

Institute of Liver and Biliary Sciences, New Delhi

India

Management of Portal Hypertension in Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is rapidly increasing and is quite often associated with cirrhosis and portal hypertension. It affects the treatment options and outcomes in cirrhosis patients. It is not clear whether presence of clinically significant portal hypertension (CSPH) with a hepatic vein pressure gradient (HVPG) of >10 mm Hg is associated with higher risk of HCC development. Use of non-selective betablockers not only reduce the incidence of variceal bleeding but probably also the incidence of HCC.

Acute variceal bleed 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 to rule in CSPH. However, an UGI endoscopy should be performed in all HCC patients. Intervention procedures such as repeated TACE and TARE are likely to increase the HVPG 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 in HCC patients 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 in liver function in patients with ascites and allowed 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 are also pending, as are their impacts on PHT.

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 being in the blood vessels.

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. A personalized and multidisciplinary management is desirable for achieving 50% two year survival in patients of HCC and portal hypertension.

Special Lecture 2

Dr. George K.K. Lau
Chairman and Senior Consultant in Gastroenterology and Hepatology,
Humanity and Health Medical Group,
Hong Kong SAR, China

Systemic Therapy for Hepatocellular Carcinoma-2023 and Beyond

In 2023, across Asia-Pacific region, unresectable hepatocellular carcinoma (uHCC) due to chronic hepatitis B (CHB) or chronic hepatitis C (CHC) remains the major cause of morbidity and mortality. Indeed, there is a high and rising prevalence of uHCC with an estimated 410,000 annually in Eastern Asia. In the past few years, with the deciphering of key molecular carcinogenic pathway and identification of the relevance of host immunity in HCC, new targeted and immune-checkpoint inhibitors (ICIs) have been made available which can markedly prolonged overall survival with quality life of the patients with uHCC. In some of these patients, uHCC can even be down-staged to be manageable by surgery or liver transplantation. Globally, with the support of large-scale randomized phase 3 clinical studies, new therapies apart from sorafenib such as lenvatinib, atezolizumab + bevacizumab have been approved as first-line therapy. In China, donafenib and sintilimab+IBI305 have also been approved as first-line therapy. For those who failed first-line therapy, new second-line therapies such as regorafenib, pembrolizumab, cabozantinib, ramucirumab and apatinib can be used. Recently, based on HIMALAYA study, STRIDE (Tremelimumab 300 mg x 1 dose + durvalumab 1500 mg every 4 weeks) has been approved globally as first line therapy for uHCC, with a 4-years overall survival (OS) of 25.2%. The median OS was found to be much higher in Asian, especially Chinese. In contrast to general concern, the immune-mediated adverse events related to STRIDE, are usually mild and manageable. In the future, one would expect to see new ICIs and targeted therapy to bring a hope of “CURE” to those with uHCC.

Special Lecture 3

Dr. Jia-Horng Kao
Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine
Department of Internal Medicine, National Taiwan University Hospital
Taiwan

Development of HCC in HBV Patients

Hepatitis B virus (HBV) is responsible for more than 50% of hepatocellular carcinoma (HCC) in HBV hyperendemic areas, such as the Asia-Pacific region. Several hepatitis B viral factors are involved in HBV-related hepatocarcinogenesis. Hepatitis B viral load is the most important risk factor of HCC development. In addition, HBV integration, HBV genotype C, and core-promoter mutations are also associated with a risk of HCC development. For untreated chronic hepatitis B (CHB) patients, the estimated HCC incidence rates per 100 patient-years were 0.03–0.17 in inactive carriers, 0.07–0.42 in asymptomatic carriers, 0.12–0.49 in chronic hepatitis, and 2.03–3.37 in cirrhosis. Complementary to HBV DNA, serum levels of the hepatitis B surface antigen and hepatitis B core-related antigen (HBcrAg) can predict the occurrence of HCC for untreated patients with low and intermediate viral loads, respectively. For patients receiving antiviral therapy, the risks of HCC occurrence 40–60% lower than those for untreated patients. Patients treated with residual detectable HBV DNA or intrahepatic cccDNA still have a risk of HCC. Serum levels of HBcrAg, M2BPGi and fibrosis-4 are predictive of the risk of HCC development in treated patients. Several well-developed HCC risk scores can help clinicians identify high-risk CHB patients for HCC surveillance, regardless of treatment status. These strategies can help minimize the threat of HCC and prolong survival in CHB patients.

Special Lecture 4

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

All Stages of HCC Patients Benefit from Systemic Therapy Combined with Locoregional Therapy

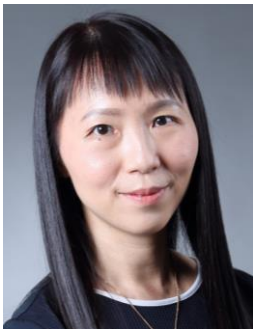
Recent advances in systemic therapy for hepatocellular carcinoma (HCC) have been remarkable. Systemic therapies were initially developed for advanced HCC. Today, sorafenib, lenvatinib (LEN), atezolizumab plus bevacizumab, durvalumab plus tremelimumab, and durvalumab alone are approved as first line agents. Regorafenib, ramucirumab, and cabozantinib have been approved as second line agents globally.

The goal of treatment in intermediate-stage HCC is achieving “cancer-free with drug-free” status. Therefore, for transarterial chemoembolization (TACE)-unsuitable patients, upfront systemic therapy with lenvatinib or atezolizumab plus bevacizumab may be initiated. After achieving normalization of abnormal vessels or tumor shrinkage, TACE may be effective. A proof-of-concept study of intermediate stage HCC with a high tumor burden showed that LEN-TACE is more effective than TACE alone, as suggested by a comparative analysis after adjusting for baseline characteristics in both treatment arms using propensity score matching. LEN-TACE sequential therapy was tested in a single arm Phase II trial, TACTICS-L, which demonstrated a favorable progression-free survival (PFS) and OS. The REPLACEMENT trial, a multicenter prospective single arm Phase II study, confirmed the efficacy of atezolizumab plus bevacizumab in a population that exceeded the up-to-seven criteria. Atezolizumab plus bevacizumab followed by curative (ABC) conversion therapy was assessed in a multicenter proof-of-concept study and validated in a population that exceeded the up-to-seven criteria. This multicenter proof-of-concept study showed that clinical complete response (CR) and drug-free status could be achieved in patients at the intermediate stage.

The IMbrave050 study, a global Phase III trial that was recently presented at the American Association for Cancer Research (AACR) meeting, showed that atezolizumab plus bevacizumab as adjuvant therapy after resection or ablation was effective in preventing recurrence mainly in early-stage HCC.

Thus, the synergistic effects of sequential/combination systemic therapy and locoregional therapy provide clinical benefits including OS prolongation in early-stage, intermediate-stage, and advanced-stage HCCs.

Keynote Lecture 1



Dr. Grace L.H. Wong
Medicine and Therapeutics, The Chinese University of Hong Kong
Hong Kong SAR, China

Strategies for preventing NASH-derived HCC

The incidence of NASH-derived HCC has increased dramatically over the last decade. Key risk factors for NASH, including IR, obesity, metabolic syndrome, and chronic inflammation, play pivotal role in hepatocarcinogenesis in NASH-derived HCC. Risk stratification and specific strategies targeting these risk factors are crucial in preventing NASH-derived HCC. Lifestyle modification and weight loss remains the only evidence-based way to prevent or delay the transition from NASH to HCC. FDA-approved drugs for NASH are yet to be available. Aspirin, metformin, pioglitazone, and statins are the few medications, which have been shown to modulate risk factors and oncogenic pathways in NASH-derived HCC, suggesting their potential for inclusion in prevention strategies.

Keynote Lecture 2

Dr. Gregory J. Gores
Mayo Clinic, Gastroenterology and Hepatology
USA

Cholangiocarcinoma: Seeking a Cure

Recent advances have occurred in the scientific understanding and clinical management of cholangiocarcinoma (CCA). The cellular immune landscape of CCA has been examined, and subsets characterized using molecular approaches. An “immune-desert” subset, relatively devoid of immune cells, has been identified suggesting immunotherapy approaches will need to take this into account. Progress has also occurred in identifying the complex heterogeneity and diverse function of cancer associated fibroblasts (CAF) in this desmoplastic cancer. Assays measuring circulating cell-free DNA (cfDNA) and cell-free tumour DNA (ctDNA) are emerging as a clinical tool for disease detection and monitoring. Targeted therapy has now become a reality as two drugs targeting fibroblast growth factor receptor 2 (FGFR2) aberrations, and one drug inhibiting isocitrate dehydrogenase 1 (IDH1) gain of function mutations are clinically available. In contrast, immunotherapy with checkpoint inhibitors for CCA has been disappointing highlighting the need for additional immune based strategies. Finally, liver transplantation for early intrahepatic CCA within protocols is a viable therapeutic option for selected patients. This overview highlights and provides in depth information on this progress and will highlight future directions both from a scientific and a clinical perspective.

Keynote Lecture 3

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

Biomarker-based Precision Medicine in the Era of Combination Immunotherapy in HCC

Treatment for advanced hepatocellular carcinoma (HCC) has entered a new era with the advent of immunotherapy. Treatment options have shifted from conventional therapy based on multi-kinase inhibitors (MKIs) to combination immunotherapy based on immune checkpoint inhibitors (ICIs). Currently, both anti-PD-L1/anti-VEGF antibody combination therapy (atezolizumab/bevacizumab, referred to as Atezo/Bev) and anti-PD-L1/anti-CTLA-4 antibody combination therapy (durvalumab/tremelimumab, referred to as STRIDE) are recommended by guidelines as first-line therapy and the other six regimens, including various MKIs, are considered second-line or later. Meanwhile, responses to any of these regimens are achieved in up to 30% of patients, and immunotherapy is associated with a certain frequency of severe irAEs. Appropriate use of these regimens may be important to prolong the prognosis of patients with advanced HCC, but there are no clear biomarkers to guide the actual use of these regimens.

Molecular and cellular biomarkers reported predicting response to Atezo/Bev for HCC include MRI-identifiable tumor steatosis, immune-related gene signatures based on tumor transcriptome, and intratumoral CD8+ T-cell infiltration as predictors of good response, and high serum IL-6 levels and the high ratio between intratumor effector T cells and regulatory T cells as predictors of poor response. Regarding clinical factors, a combined AFP, CRP, and mALBI grade combined scores have also been reported to be useful in predicting response. In addition, we also reported that ctDNA profiling may also help stratify the prognosis of hepatocellular carcinoma patients treated with Atezo/Bev. On the other hand, there is no biomarker that distinguishes Atezo/Bev from STRIDE. Because the two regimens differ in some of their points of action on the cancer immune cycle. Therefore, an appropriate understanding of each patient's cancer immune status may be helpful in drug selection.

In this lecture, I will outline the biomarkers for combined immunotherapy that have been reported so far, including our findings, and discuss future perspectives.

Keynote Lecture 4

Dr. Man-Fung Yuen
Department of Medicine, School of Clinical Medicine,
The University of Hong Kong,
Hong Kong SAR, China

Strategies for Terminating HBV Related HCC

As chronic hepatitis B (CHB) infection remains to be a globally prevailing disease, hepatocellular carcinoma (HCC) is still a major health threat worldwide. Same to all kinds of cancer-causing virus infections, primary prevention of infection through universal vaccination is the most effective strategy in terminating hepatitis B virus (HBV) related HCC. It has been shown that HCC rate is dramatically decreasing in many countries where universal HBV vaccination has been implemented decades ago. However, there is still a large population of existing CHB patients who still have a considerable risk of developing HCC in their later lives. Secondary prevention by suppressing the virus replication by the current treatment with nucleos(t)ide analogs (NA) in CHB patients is accompanied by more than 40% risk reduction of HCC. The degree of HBV DNA suppression correlates with the risk reduction of HCC. More than 95% of patients receiving 5 years of NA would have undetectable HBV DNA levels by standard assays with lower limit of detection of 10 IU/mL. A recent study however, further showed that patients with residual detectable HBV DNA and HBV RNA by highly sensitive assays had a comparatively higher risk of HCC development. It suggests that maximal viral nucleic acid suppression by additional and/or more potent antiviral agents would be associated with a further risk reduction of HCC development. Furthermore, studies had shown that achieving HBsAg seroclearance (functional cure) at the age before 50 years or at the time before establishment of cirrhosis was associated with a reduced risk of HCC. Therefore, novel agents enhancing early-aged functional cure rate, not only allows patients to cease the long-term NA treatment, it should theoretically also be associated with a lower risk of HCC development in chronic hepatitis B patients.

Keynote Lecture 5

Dr. Henry Lik Yuen Chan
Department of Internal Medicine, Union Hospital
Faculty of Medicine, The Chinese University of Hong Kong
Hong Kong SAR, China

Deciphering HCC Risk Scores for Chronic Hepatitis B

Hepatocellular carcinoma (HCC) is a major cause of morbidity and mortality associated with chronic hepatitis B virus (HBV) infection. In previous studies, various risk factors have been found to increase the risk of HCC, including host factors (age and gender), virus factors (HBeAg, HBsAg, HBV DNA), liver disease factors (liver cirrhosis, elevated ALT, low platelet, low serum albumin and elevated serum bilirubin), and co-morbid illnesses (diabetes mellitus and alcoholism). Due to the complicated interaction of these factors, HCC risk scores have been developed based on large patient cohorts to estimate the risk of HCC. In general, HCC risk scores are summation of weighted independent risk factors to classify patients into different strata of HCC risk over a period of a few years. However, most research groups have not assessed the role of their risk score in prevention of HCC, namely decision on antiviral therapy (risk reduction) and HCC surveillance (prognosis improvement).

The first HCC risk scores are derived in Hong Kong and Taiwan based on longitudinal untreated patient cohorts. The most widely used scores are CU-HCC score, GAG-HCC score and REVEAL-HCC score. These scores have been both internally and externally validated. One issue of these score is heavy weight of liver cirrhosis, which can sometimes be difficult to determine. A LSM-HCC score has been developed based on transient elastography, and has been shown to perform better than CU-HCC score to predict risk of HCC.

For patients undergoing nucleos(t)ide analogue (NA) treatment, theoretically all of them have significant risk of HCC and should undergo regular HCC surveillance. However, some patients might have HCC risk reduced and fibrosis regressed after NA therapy. The HCC risk score developed in untreated patients in Asia has been found unsatisfactory to predict HCC risk among patients on NA. The most validated risk score for NA-treated patients is the PAGE-B score developed in Europe. In multiple cohorts across the world, patients with low PAGE-B score have an estimated annual HCC risk of <0.2%, which is not cost-effective for HCC surveillance. In concordance to the EASL Clinical Practice Guideline, non-cirrhotic patients with low PAGE-B score can be considered exempt from HCC surveillance. However, the performance of PAGE-B score among cirrhotic patients is still suboptimal. Other risk scores which integrate liver stiffness measurement or liver cirrhosis are also derived in Asia to predict HCC risk in Asian patients.

Keynote Lecture 6

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

Molecular Mechanisms and Cellular Origins of Biliary Tract Cancer: Cutting-Edge Knowledge from Mouse Models

The cellular origin of cholangiocarcinoma is a topic of interest. With regard to extrahepatic cholangiocarcnoma (ECC), peribiliary glands (PBGs), a potential stem cell niche of biliary epithelial cells (BECs), have attracted attention as the cellular origin of ECC. We recently established a new mouse model of ECC through CK19-positive duct-cell-specific activation of Kras and deletion of TGFβR2 and E-cadherin. In this mouse model, BECs are detached and died due to loss of E-cadherin, which induces chronic inflammation in the bile duct. Careful analysis of histology revealed that PBG became gradually dysplastic during inflammation and eventually develop to cholangiocarcinoma. However, to definitely prove that PBG is cellular origin of biliary tract cancer, animal experiments using a PBG-specific gene recombination system was required. Therefore, we sought to identify PBG-specific markers and found that Axin2, a target gene of the Wnt /β-catenin pathway, expressed specifically in PBGs of periampullary region. Genetic lineage-tracing revealed that Axin2+ periampullary PBG cells function as biliary epithelial stem cells. Of note, deletion of PTEN in periampullary PBG cells gave rise to ampullary carcinoma which was suppressed by Wnt inhibitor. Therefore, Wnt signaling is a potential therapeutic target for ampullary carcinoma. Furthermore, we have established additional mouse models of extrahepatic cholangiocarcinoma by combining different genetic abnormalities and identified lipid metabolic reprogramming as a potential therapeutic target. In this session, I will introduce a part of that data.

Keynote Lecture 7

Dr. Mindie H. Nguyen
Division of Gastroenterology and Hepatology
Stanford University Medical Center
USA

Strategies for Terminating HCV-related HCC

Effective and safe oral direct acting antiviral (DAA) medications for the treatment of chronic hepatitis C virus (HCV) infection have been available for almost 10 years; however, many people with HCV infection remain undiagnosed, and many people with active HCV infection remain untreated. Consequently, there are missed opportunities to prevent many HCV-related HCC cases since DAA treatment has been well proven to significant decrease the development of HCC. Additionally, new HCV infection is on the rise in some populations due to illicit drug use such as those affected by the opioid epidemic in the United States. Therefore, to terminate HCV-related HCC, there should be a "multiple-prong" approach that includes (1) prevention of new HCV infection, (2) timely screening and diagnosis of the undiagnosed infected pool, and (3) timely DAA treatment of people with known viremic HCV infection to prevent disease progression such as HCC.

It is also important to note that people with cured HCV infection who have advanced liver fibrosis or cirrhosis remain at risk for HCC. These individuals should continue to undergo HCC surveillance to promote early diagnosis of HCC, curative treatment and decreased the mortality burden of HCV-related HCC.

Lastly, people with HCC diagnosed in the setting of active HCV infection should also be considered for DAA therapies which have also been well documented to improve liver-related and overall survival in HCV-related HCC. In HCV-infected patients with inactive HCC, the sustained virologic response (SVR) rate to DAA can be expected to be similar to non-HCC patients, though the SVR rate in patients with active HCC is still fairly high (85%). Thus, to optimize SVR rate, it is generally advisable to initiate DAA treatment after adequate treatment for HCC.

Keynote Lecture 8

Dr. Tushar Patel
Department of Transplantation, Division of Gastroenterology and Hepatology, Mayo Clinic Florida
USA

RNA Therapeutics for Liver Cancers

RNA therapeutics have emerged as a promising approach for the treatment of liver cancers, offering new avenues for targeted therapies. Liver cancer, including hepatocellular carcinoma (HCC), remains a major global health concern with limited treatment options and a high mortality rate. RNA-based therapeutics are of interest for the treatment of HCC as they can specifically target cancer cells, modulate gene expression, alter cell signaling and can modulate immune responses. Several preclinical studies have shown promising results for the use of RNA therapeutics for HCC.

There are several types of RNA therapeutics. These include the use of small interfering RNA, short hairpin RNA, microRNA replacement, anti-microRNA and antisense oligonucleotides, and messenger RNA. Synthetic or biological nanoparticles (such as extracellular vesicles) provide a means to efficiently deliver RNA therapeutics to liver cancer cells. These nanoparticles can protect the RNA from degradation and improve their uptake into target cells. The use of targeted delivery systems holds great promise for enhancing the efficacy and reducing off-target effects of RNA therapeutics.

This emerging field will be reviewed, with examples of targeted RNA therapies for HCC and discussion of key steps in therapeutic development. The challenges faced with developing RNA therapeutics and their delivery will be discussed along with potential approaches to address these in the future.

APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Abstracts

Sponsored Seminars

Luncheon Seminar 1 (Sponsored by Eisai Co., Ltd. / MSD K.K.)

Dr. Takeshi Terashima
Department of Gastroenterology, Kanazawa University Hospital, Japan

Positioning of Lenvatinib and Role of Adding Hepatic Arterial Infusion Chemotherapy to Lenvatinib for Unresectable Hepatocellular Carcinoma in Era of Immunotherapy

Lenvatinib is an oral small molecule inhibitor of receptor tyrosine kinase inhibiting the kinase activities of vascular endothelial growth factor receptors, fibroblast growth factor receptors, KIT and RET. A global phase III trial, REFLECT, which was open-label, multicenter, non-inferiority trial to verify the efficacy and safety of lenvatinib compared to sorafenib, included the unresectable hepatocellular carcinoma (HCC) patients without prior systemic treatment. Afterwards, a phase II trial, LEOPARD, to evaluate the efficacy and safety of lenvatinib in combination with hepatic arterial infusion chemotherapy using cisplatin revealed objective response rate as assessed by the RECIST were 45.7 (28.8-63.4) %. Immunotherapy consisting of atezolizumab and bevacizumab or durvalumab and tremelimumab was shown to be useful, and has currently been established as the first line treatment for unresectable HCC. Lenvatinib and other molecular targeted agents as well as hepatic arterial infusion chemotherapy still has a role to play in the long-term prognosis of patients. I will introduce the clinical trial results and our experience under clinical practice of lenvatinib and LEOPARD regimen, and hope to have an opportunity for discussing some issues for patients with HCC.

Luncheon Seminar 1 (Sponsored by Eisai Co., Ltd. / MSD K.K.)

Dr. Kaoru Tsuchiya
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Musashino Red Cross Hospital (MRCH),
Japan

New Treatment Strategies for Unresectable HCC ~The Positioning of Lenvatinib in Real-world Practice~

Recently, 8 regimens for unresectable hepatocellular carcinoma (HCC) were approved in Japan. As first-line treatment, immuno-combination therapies, including atezolizumab plus bevacizumab and durvalumab plus tremelimumab, are recommended in patients without contraindications for checkpoint inhibitors. Lenvatinib is a multi-kinase inhibitor that also expects to work for the modification of tumor microenvironments. Moreover, effects on vascular properties in tumor tissue by lenvatinb was already reported in some studies. In a clinical setting, the usefulness of the combination of lenvatinib and locoregional therapy has been reported, including the TACTICS-L study, LEOPARD study, and LAUNCH study. According to the results of the LAUNCH study, the combination therapy, lenvatinib plus TACE, was significantly better both in patients with and without extrahepatic metastasis compared to lenvatinib alone. The LEOPARD study, the combination of lenvatinib plus HAIC with CDDP, revealed that objective response rate (ORR) and disease control rate (DCR) based on RECIST1.1 were 45.7 and 83.3%. Especially in patients with VP3 or VP3, the efficacy of immunotherapy may be limited, and the median OS and PFS in patients with VP4 treated with atezolizumab plus bevacizumab were 7.6 and 5.4 months. Lenvatinib plus HAIC (CDDP) would be considered in such a population. Most adverse events associated lenvatinib, including fatigue, appetite loss, hypertension, and diarrhea, are dose-dependent. In the TACTICS-L study, the relative dose intensity of lenvatinib after TACE was not associated with a complete response (CR) and ORR. In contrast, a full dose of lenvatinib before TACE was a significant factor associated with CR and ORR. In real-world practice, we should modify the dose of lenvatinib based on the treatment situation, age, and liver function. The successful conversion resection after achieving an objective response by systemic therapy has been increasing, and we should consider the regimen based on ORR, time to response, half-time, and patient's background.

Luncheon Seminar 2 (Sponsored by Chugai Pharmaceutical Co., Ltd.)

Dr. Sadahisa Ogasawara
Department of Gastroenterology,
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Chiba University,
Japan

Unlocking the Potential of Combination Immunotherapy in Advanced Hepatocellular Carcinoma

Over two years have passed since the introduction of atezolizumab plus bevacizumab for advanced hepatocellular carcinoma (HCC) in Japanese clinical practice. Notably, the Phase III trial (IMbrave 150) results have been consistently replicated in terms of efficacy. However, a slight concern has arisen regarding safety due to higher rates of proteinuria associated with bevacizumab in actual clinical practice, especially among patients with concomitant lifestyle-related diseases in Japan. Nevertheless, appropriate management strategies are being shared and considered feasible. Efforts to identify patient populations that can benefit from this combination therapy have led to the exploration of biomarkers using diverse clinical data and specimens. Although no definitive indicators have been presented, intriguing data are emerging daily. The advent of atezolizumab plus bevacizumab holds the potential to enable the transition to curative therapy, which was nearly impossible with conventional drug therapies. The ultimate goal and dream for patients with advanced HCC are to achieve freedom from both cancer and systemic therapy. Encouragingly, many cases have demonstrated that the combination of atezolizumab plus bevacizumab can lead to cancer remission and discontinuation of treatment (so called “cancer free and drug free”). Looking ahead, collaboration with surgeons and radiologists to explore appropriate approaches and curative treatment options will be crucial for improving outcomes of advanced HCC patients in the future.

Luncheon Seminar 3 (Sponsored by Gilead Sciences K.K. Medical Affairs)

Dr. Masayuki Kurosaki
Executive Vice-President of Musashino Red Cross Hospital,
Director of the Department of Gastroenterology and Hepatology,
Musashino Red Cross Hospital,
Japan

Recent Topics about Hepatocellular Carcinoma: Focusing on Risks of Hepatitis and Advances in the Therapy

Hepatitis B and C remain important as background for hepatocellular carcinoma (HCC). Appropriate antiviral therapy and identification of high-risk cases for HCC are important issues. Anti-PD-1 plus anti-VEGF or anti-CTLA4 has become a standard of 1st line therapy for unresectable HCC. Question remains on the selection of regimens after progress disease, or the timing of conversion therapy for those with favorable response. These points will be discussed.

Luncheon Seminar 4 (Sponsored by AbbVie GK)

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

Multidisciplinary Treatment including DEB -TACE Combined with HAIC and iCIs should be Considered to Control HCC ~Including Patients after DAA Treatment~

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 iCI treatment for the HCC patients.

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

Dr. Jun Inoue
Department of Gastroenterology, Tohoku University Hospital,
Japan

A New Era in Liver Diseases:
Recent Advances and Issues in Hepatitis C Virus Infection and Liver Cancer

Highly effective treatments, direct-acting antivirals (DAAs), have become available for hepatitis C virus (HCV) infection, but several issues remain to be addressed. Even after HCV is eradicated, the risk of hepatocellular carcinoma (HCC) remains, and decompensation events such as variceal rupture and hepatic encephalopathy can occur in patients with cirrhosis. Regular surveillance for HCC and follow-up of portal hypertension are required, but it is economically important to identify high-risk patients. It is also assumed that many HCV-infected patients have not been tested for HCV antibody and that there is a significant number of patients who have been found to be infected with HCV but have not been treated with DAAs.

Several chemotherapy options are now available for HCC, including immune checkpoint inhibitors, and an appropriate choice for each patient is important. This seminar will discuss recent advances and the clinical issues in HCV infection and HCC.

APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Abstracts

Workshops

Workshop 1 [Systemic Chemotherapy & Oncology 1]
WS1-1 10072

Multimodal Treatment Strategy with Atezolizumab plus Bevacizumab Towards the Complete Response in Unresectable Hepatocellular Carcinoma

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Background: Atezolizumab plus bevacizumab (Atez/Bev) treatment has brought the new era of combination therapy for unresectable hepatocellular carcinoma (uHCC). Due to the inter-patient heterogeneity on tumor status, the treatment strategy should be maximumly optimized for each patient. We here report the uHCC cases who could be successfully converted into the curable status through the multidisciplinary strategy.
Method: We examined the clinical characteristics and treatment outcome of 81 patients with uHCC treated with Atez/Bev in our hospital before June 2023. We focused on the cases who could achieve the cancer-free status by the multimodal treatment strategy with Atez/Bev.
Results: The best response was CR/PR/SD/PD/NE in 2/26/31/20/2 by RECIST1.1 and objective response rate was 34.6%. Among them, four cases (Case1 with BCLC-C and Case2-4 with BCLC-B) experienced the conversion therapy with surgery or ablation. Case 1 had huge liver tumor with the maximum diameter of 92mm and hepatic vein invasion (Vv2). The best response after 6 courses of Atez/Bev was PR, and the surgical specimens demonstrated pathological CR. Notably, Cases 3 and 4 could achieve CR by radiofrequency ablation after Atez/Bev. In addition, three cases with far-advanced uHCC (Cases 5-7, with huge lung metastasis with left atrium invasion, peritoneal seeding around rectum, and right atrium invasion, respectively) have become resectable status after Atez/Bev followed by intensive treatment with hepatic arterial infusion chemotherapy, trans-arterial chemoembolization or radiation therapy.
Conclusion: Atez/Bev-based multimodal treatment strategy has brought us the possibility to achieve the cancer-free status not only in the intermediate-stage but also far-advanced uHCC patients.

Workshop 1 [Systemic Chemotherapy & Oncology 1]
WS1-2 10119

Late Line Treatment with Atezolizumab plus Bevacizumab Therapy is Less Effective in Unresectable Hepatocellular Carcinoma

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Background: Atezolizumab plus Bevacizumab (ATZ+BV) therapy became the first line treatment for unresectable hepatocellular carcinoma. However, ATZ+BV is sometimes chosen as late line treatment when other TKIs fail to work. We investigated the treatment outcomes of a multicenter retrospective study of ATZ+BV therapy in the late line.
Methods: We enrolled 218 patients (146 in the first-line group and 72 in the late-line) with unresectable hepatocellular carcinoma above BCLC stage B from October 2020 to December 2022 at eight Japanese centers 1) We compared clinical background, and best overall response. 2) Inverse probability of treatment weighing (IPTW) was used to adjust for background factors in both groups, and progression free survival (PFS) was compared with these two groups.
Results: 1) Median age was 72.3 years. BCLC stage was shown B/C=78/140. mALBI grade was 1/2a/2b/3=58/64/92/4. The best overall response rate was 50.8% in the first-line and 20.2% in the late-line. 2) PFS was significantly higher in the first-line than in the late-line, 10.5 months and 4.1 months. IPTW analysis showed that the duration of PFS was significantly shorter in the late-line with 3.7 months and 7.7 months in the first-line.
Conclusion: We found that ATZ+BV therapy in the late line was associated with poorer outcomes compared to the first line. ATZ+BV therapy should be used more aggressively in patients who require chemotherapy. If ATZ+BV is used in the late line, the possibility of failure of response should be taken into consideration and the next treatment should be prepared as early as possible.

Workshop 1 [Systemic Chemotherapy & Oncology 1]
WS1-3 10046

Comparative Analysis of Atezolizumab plus Bevacizumab and Hepatic Artery Infusion Chemotherapy in Unresectable Hepatocellular Carcinoma: A Multi-center, Propensity Score Study

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Pil Soo Sung[1], Jeong Won Jang[1], Jong Young Choi[1], Si Hyun Bae[2], Seung Kew Yoon[1]

Background: The purpose of this study was to compare the prognosis and characteristics of the advanced HCC patients treated with the first-line combination therapy and hepatic artery infusion chemotherapy.
Method: We retrospectively assessed 174 patients treated with HAIC and 77 patients treated with atezolizumab/bevacizumab combination therapy between 2018 and 2022 in 5 university-affiliated hospitals in Korea. Firstly, we assessed the overall survival (OS), progression free survival (PFS), objective response rate (ORR) and disease control rate (DCR) between atezolizumab/bevacizumab combination therapy and hepatic artery infusion chemotherapy.
Results: When we compared the baseline characteristics of the enrolled patients, we found that there were significant differences in age, tumor numbers, portal vein invasion and Child Pugh scores. HAIC treated patients were significantly younger, had significantly more single number of tumors, had more portal vein invasions and had worse Child-Pugh scores. Even though HAIC-treated patients had more portal vein invasions and worse Child-Pugh scores, however, there was no significant difference in overall survival or progression-free survival between the two groups. After adjusting for bias that could occur due to confounding variables by PSM method, patients treated with Ate/beva therapy has a significantly longer OS than patients treated with HAIC ($P<0.05$), although there were no significant differences in progression-free survival and objective responses.
Conclusion: According to our multi-center, propensity score study, patients treated with Ate/beva therapy has a significantly longer OS than patients treated with HAIC.

Workshop 1 [Systemic Chemotherapy & Oncology 1]
WS1-4 10105

Changes in Serum Growth Factors During Resistance to Ate-zolizumab Plus Bevacizumab Treatment in Patients with Un-resectable Hepatocellular Carcinoma

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The possible mechanisms of resistance to atezolizumab/bevacizumab for unresectable HCC and the subsequent response to these therapies remain underexplored. The sequential changes in se-rum growth factors, including VEGF-A, VEGF-C, VEGF-D, ANG-2, FGF-19, HGF, and EGF during atezolizumab/bevacizumab for unresectable HCC were evaluated in 46 patients. Patients who experienced PD after CR, PR, or SD to atezolizumab/bevacizumab were evaluated. A total of 4, 9, 19, and 14 patients showed CR, PR, SD, and PD, respectively. Of 32 patients with disease control, 27 experienced PD after CR, PR, or SD with atezolizumab/bevacizumab. Baseline growth factor levels were similar between patients with or without disease controls and those with or without objec-tive-response. Growth factor changes between the baseline and best response points (BRP) for patients with disease control showed that FGF-19 significantly increased and ANG2 significantly decreased at the BRP. Growth factor changes between the BRP and the PD point in 27 patients who experienced PD after disease control showed that VEGF-D and ANG2 significantly increased at the PD point compared with that at BRP. Summarily, increased serum VEGF-D and ANG-2 levels might contribute to developing resistance to atezolizumab/bevacizumab for unresectable HCC and might be a target molecule in subsequent salvage therapies.

Predictive Factors for Durable Response in Patients Received Atezolizumab plus Bevacizumab Therapy for Unresectable Hepatocellular Carcinoma

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Background: With the emergence of combination therapy which does not inhibit vascular endothelial growth factor (VEGF), the optimal strategy of sequential treatment for hepatocellular carcinoma (HCC) is under debate. Biomarkers that predict patients who benefit from VEGF-inhibiting treatment are urgent unmet needs. We aimed to clarify the predictive factors for the efficacy of atezolizumab plus bevacizumab (Atez+Bev).
Methods: We retrospectively analyzed 103 consecutive patients with unresectable HCC who received Atez+Bev. The radiological response was evaluated by RECIST ver 1.1 at 6-8 weeks from Atez+Bev initiation and every 8-12 weeks thereafter. The peripheral blood VEGF at baseline and 3-6 weeks were analyzed. The durable response was defined as a maintained response (CR/PR/SD) > 6 months and received Atez+Bev >6 months.
Results: Median overall survival (OS) was 24.4 months, while progression-free survival (PFS) was 5.7 months. Among patients who achieved disease control (75%), the durable response was 40.5% in 1st-line treated patients, which was significantly higher than 18.0% in 2nd or later-line treated patients (p=0.02). Predictive factors for durable response at baseline were BCLC stage B (Odds ratio (OR) 3.2, 1.4-7.4, p=0.007) and 1st line treatment (OR 2.7, 2.2-6.5, p=0.02). Where on-treatment factors up-to 6 weeks were included, AFP response (OR 3.0, 1.2-7.6, p=0.02) and on-treatment VEGF <97pg/ml (OR 2.7, 1.1-7.0, p=0.03) were independent factors associated with the durable response along with BCLC stage and treatment line.
Conclusion: Durable response was significantly higher in 1st-line treated patients. Peripheral blood VEGF decrease during Atez+Bev treatment can be a biomarker to define durable responder.

Workshop 2 [Systemic Chemotherapy & Oncology 2]
WS 2-1 10128

A Prospective Study to Assess the Safety and Efficacy of Lenvatinib in Patients with Advanced Hepatocellular Carcinoma Aiming to Maximise Its Potential in Current Clinical Practice

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Background: This study aimed to assess the safety and efficacy of lenvatinib in real-world practice, including specific patients that were excluded from the REFLECT trial.
Methods: This multicenter, nonrandomized, open-label prospective study was conducted at 10 medical facilities in Japan (jRCTs031190017). Eligible patients had advanced HCC and were suitable for lenvatinib treatment. The study encompassed patients with high tumor burden (with >50% intrahepatic tumor volume, main portal vein invasion, or bile duct invasion), Child-Pugh B status, and considering lenvatinib as second-line treatment following atezolizumab plus bevacizumab.
Results: From December 2019 to September 2021, a total of 59 patients were analyzed, with 47 classified as Child-Pugh A and 12 as Child-Pugh B. Among patients with Child-Pugh A, a high occurrence of aspartate aminotransferase elevation was observed in cases with high tumor burden. No other significant adverse events (AEs) were detected even in second-line treatment. However, patients with Child-Pugh B exhibited high frequency of grade 3 or higher AEs and discontinuation rate due to AEs compared to patients with Child-Pugh A. Median overall survival was 19.7 and 4.1 months in Child-Pugh A and B, respectively. Lenvatinib plasma concentration was found to be higher in Child-Pugh B patients on days 8 and 15, and higher concentration correlated with adjustment in dosage and reduced relative dose intensity.
Conclusions: Lenvatinib is safe and effective for advanced HCC in patients with Child-Pugh A in real-world settings. However, our study does not strongly recommend lenvatinib for patients with Child-Pugh B.

Workshop 2 [Systemic Chemotherapy & Oncology 2]
WS2-2 10137

Prognostic Factors for Survival in Patients with Intermediate-stage Unresectable Hepatocellular Carcinoma Treated with Lenvatinib or Atezolizumab plus Bevacizumab

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Background: Previously, the main treatment for intermediate-stage hepatocellular carcinoma(HCC)was TACE. However, the concept of “TACE refractory” or “TACE unsuitable” was recently established, and the clinical usefulness of systemic therapy in BCLC stage B has been reported. In this study, we investigated the prognostic factors for survival in patients with intermediate-stage HCC who received lenvatinib(LEN)or atezolizumab plus bevacizumab therapy (AB)in real-world practice.
Methods: The patients who had BCLC stage B HCC beyond up to 7 (UTS) criteria and received LEN (n=47) or AB (n=53) at our hospital were included. The overall survival (OS) and progression-free survival (PFS) were analyzed retrospectively using the Kaplan-Meier method.
Results: Median OS was 22.8 months for LEN and 20.5 months for AB, median PFS was 6.2 months for LEN and 8.1 months for AB. In univariate analysis of the LEN group, baseline ALBI score, AFP <400 ng/mL, and peripheral blood neutrophil/lymphocyte ratio (NLR) were significantly associated with OS. In multivariate analysis of the LEN group, baseline ALBI score and baseline NLR were significant independent factors. The only significant factor associated with OS in the AB group was the pre-treatment ALBI score. Neither the maximum intrahepatic tumor diameter nor the number of tumors was a factor contributing to OS in either the LEN or AB groups.
Conclusion: In BCLC stage B and UTS-out patients, maximum tumor diameter and number of tumors were not predictors for OS. Biomarkers including NLR and tumor markers need to be further investigated.

Workshop 2 [Systemic Chemotherapy & Oncology 2]
WS2-3 10012

Immunokinetic Analysis Predicts Efficacy of Combination Immunotherapy for Advanced Hepatocellular Carcinoma

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Background: Combination immunotherapy including immune checkpoint inhibitors are used as first-line therapy for advanced hepatocellular carcinoma (HCC), but the response rate of each regimen is still insufficient. We sought to identify predictors of response to atezolizumab/bevacizumab (ATZ/BEV) combination therapy by immunokinetic analysis.
Methods: In 23 patients with advanced HCC who underwent liver tumor biopsy prior to ATZ/BEV, we performed RNA-seq of the tumor area and evaluated factors associated with treatment response. CITE-seq and TCR repertoire analysis were performed using human peripheral blood mononuclear cell (PBMC) samples from 5 responder and 5 non-responder patients before and 6 weeks after ATZ/BEV therapy to search for predictive factors for response.
Results: RNA-seq results showed that expression levels of CXCL9, CD69, and EOMES, and the frequency of Immune class was significantly higher in responders than in non-responders. Gene signature analysis showed that effector T cells were more frequent in responders, and that the Interferon and antigen-presentation (IFNAP) signature, Atezolizumab Bevacizumab response signature (ABRS), and T cell exhaustion signature were significantly higher in responders than in non-responders. PFS was significantly prolonged in patients with high ABRS compared to those with low ABRS. CITE-seq and TCR repertoire analysis showed that the frequency of several clusters and CD8 T cell clonality were different between responders and non-responders. GO analysis suggested that T cells were differentiated and activated after 6 weeks of treatment in responders.
Conclusions: In advanced HCC, the immunokinetic analysis of tumor site or peripheral blood may be able to predict response to ATZ/BEV therapy.

Workshop 2 [Systemic Chemotherapy & Oncology 2]
WS2-4 10083

Cabozantinib Therapy in Patients Previously Treated with Atezolizumab/Bevacizumab for Advanced Hepatocellular Carcinoma-Importance of Good Liver Function and Good Performance Status

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Background: The aim of this study was to investigate clinical outcomes for cabozantinib in clinical practice in patients with advanced hepatocellular carcinoma (HCC) previously treated with atezolizumab plus bevacizumab (Atz/Bev), with a focus on whether patients met criteria of Child-Pugh Class A and Eastern Cooperative Oncology Group- performance status (ECOG-PS) score 0/1 at baseline.
Methods: Eleven patients (57.9%) met the criteria of both Child-Pugh class A and ECOG-PS score 0/1 (CP-A+PS-0/1 group) and 8 patients (42.1%) did not (Non-CP-A+PS-0/1 group) were retrospectively evaluated efficacy and safety.
Results: Disease control rate was significantly higher in the CP-A+PS-0/1 group (81.1%) than in the non-CP-A+PS-0/1 group (12.5%). Median progression free survival, overall survival and duration of cabozantinib treatment were significantly longer in the CP-A+PS-0/1 group (3.9 months, 13.4 months, and 8.3 months, respectively) than in the Non-CP-A+PS-0/1 group (1.2 months, 1.7 months, and 0.8 months, respectively). Median daily dose of cabozantinib was significantly higher in the CP-A+PS-0/1 group (22.9 mg/day) than in the non-CP-A+PS-0/1 group (16.9 mg/day).
Conclusions: Cabozantinib in patients previously treated with Atz/Bev has potential therapeutic efficacy and safety if patients have good liver function (Child-Pugh A) and are in good general condition (ECOG-PS 0/1).

Therapeutic Strategy for Advanced Hepatocellular Carcinoma with Combination of Systemic Therapy and Surgical Resection

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Background: The effectiveness of systemic therapy for advanced hepatocellular carcinoma using Lenvatinib (LEN) and Atezolizumab + Bevacizumab (AB) has been confirmed in clinical practice. Systemic therapy is expected to be useful in combination with curative-intent surgical resection, including preoperative treatment for conversion surgery, postoperative adjuvant therapy, and the options for patients with postoperative recurrence.
Methods: One hundred and thirty-four patients treated with LEN (N=79) or AB (N=55) for advanced hepatocellular carcinoma were analyzed. The objective response rate (ORR) was assessed based on modified RECIST.
Results: The indications for systemic therapy (partially overlapping) were intrahepatic multifocal tumor (N=87, 65%), extrahepatic metastasis (N=44, 33%), and macrovascular invasion (N=13, 10%). The patients background including liver function and tumor characteristics was similar between the groups of LEN and AB. The ORR was 48% (CR1(1%)/PR37(47%)/SD27(34%)/PD14(18%)) after LEN and 42% (CR1(2%)/PR22(40%)/SD21(38%)/PD11 (20%)) after AB. While overall survival of each group was similar, the median progression-free survival of AB (15mo) was significantly better than that of LEN (7mo). The pretreatment alpha fetoprotein level was a potential predictor for the therapeutic response to LEN or AB. Six patients underwent surgical resection after LEN(N=4) and AB(N=2). Two cases achieved pathological CR with 36- and 18-months recurrence-free survival. Twenty-nine patients with postoperative recurrence were treated with LEN and 27 patients with AB, showing response rates of 59% and 41%, and disease control rates of 86% and 70%, respectively.
Conclusion: Systemic therapy using LEN and AB was effective for advanced hepatocellular carcinoma, offering perspective for combination therapeutic strategy with surgical resection.

Workshop 3 [Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD]
WS3-1 10135

The Difference of Branched-chain Amino Acids Tyrosine Ratio (BTR) among Chronic Liver Disease Comparing to Healthy Adult

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Background and Aims: Imbalances of plasma free amino acids (PFAAs) are occurred in chronic liver diseases (CLD) as background of hepatocellular carcinoma (HCC). The aim of this study is to elucidate imbalance of PFAAs in CLD with or without HCC by comparing with healthy adults.
Methods: We retrospectively investigated blood test data and 23 PFAAs in 2529 patients with various CLD from four institutions. After setting exclusion criteria, n=1326 were finally included in the analysis. PFAAs data of 1218 healthy adults were obtained from a biobank in Japan. Patients and healthy adults were matched for gender, age, and BMI using propensity scores, and changes in liver reserve capacity (mALBI grade) and branched-chain amino acids (BCAA) and tyrosine ratio (BTR) were analyzed.
Results: We found that aromatic amino acids (AAA) were significantly increased by aging in healthy adults, and BCAA was increased by BMI, gender (men). BTR decreased with progression of mALBI grade regardless of CLD background. BTR was significantly increased in mALBI grade 1 and decreased above 2b compared to healthy adults in NAFLD/NASH. On the other hand, ALD showed a decreasing at grade 1 and a significant decrease above 2a. In other etiologies, viral CLD and AIH showed a decrease in BTR above 2a, while PBC and cryptogenic showed a decrease in BTR above 2b. Furthermore, BTR was more decreased at 2b in HCV patients with HCC than patients without HCC.
Conclusion: The decrease point of BTR is different by CLD etiology and with or without HCC.

Workshop 3 [Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD]
WS3-2 10042

Agile 3+ and Agile 4, Non-invasive Tests for Liver Fibrosis, are Excellent Formulae to Predict Liver-related Events in Nonalcoholic Fatty Liver Disease

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Background: The non-invasive tests, Agile 3+ and Agile 4, effectively identify patients with nonalcoholic fatty liver disease (NAFLD) complicated with advanced fibrosis (F3-4) and cirrhosis (F4), respectively. Little information is available on associations between Agile scores and intra-/extrahepatic events. The aim of this study was to determine the predictive performance of Agile scores for intra-/extrahepatic events in Asian patients with biopsy-proven NAFLD.
Methods: We conducted a retrospective multicenter cohort study to investigate associations between intra-/extrahepatic events and two Agile scores, Agile 3+ and Agile 4. The scores were obtained by combining clinical parameters and liver stiffness measurement using transient elastography.
Results: Among 403 enrolled patients, 11 had liver-related events (LREs), including seven with hepatocellular carcinoma. The incidence of LREs and hepatocellular carcinoma showed a stepwise increase in the advanced fibrosis group (F3-4), Agile 3+ rule-in (F3-4, highly suspected), and Agile 4 rule-in (F4, highly suspected) groups, compared to their counterparts. Hazard ratios for LREs in the advanced fibrosis group, Agile 3+ rule-in, and Agile 4 rule-in groups were 4.05 ($p = 0.03$), 23.5 ($p = 0.003$), and 45.5 ($p<0.001$), respectively. The predictive performance results for Agile 3+ and Agile 4 were 0.780 and 0.866, respectively, which were higher than for fibrosis (0.595). Unlike for LREs, Agile scores failed to identify patients with extrahepatic events, including cardiovascular events and extrahepatic cancer.
Conclusions: Agile 3+ and Agile 4 scores are excellent non-invasive tests for predicting LREs in patients with NAFLD, possibly without histological assessment.

Workshop 3 [Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD]
WS3-3 10010

Impact of Liver Fibrosis Severity on Oncological Prognosis in Hepatocellular Carcinoma: 1-to-1 Individual Case-matched Analysis

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Background: The risk of recurrence based on the fibrosis stage has not been well evaluated in hepatocellular carcinoma (HCC). This study aimed to clarify the impact of liver fibrosis severity on the cancer-specific prognosis following resection of HCC.
Methods: A total of 524 consecutive patients who had surgery for HCC were included. Recurrence-free survival (RFS) were compared according to fibrosis stage. Furthermore, one-to-one individual case-matched analysis was performed between 62 patients with F0 and those with F1-3, and 122 patients with F1–3 and those with F4 regarding recurrence prognosis.
Results: Five–year RFS was significantly worse in the F4 group than other fibrosis stages (5–year RFS for F0, F1–3, and F4: 46.6 %, 33.1 %, and 23.5 %, respectively, P&lt0.01). Multivariate analysis revealed that F1–3 and F4 were the independent poor prognosis factors. After matched analysis, RFS of the F1–3 group was significantly worse than that of the F0 group (46.8% vs. 66.1%, P=0.029), likewise, RFS of the F4 was significantly worse than that of the F1–3 group (54.9% vs. 75.4%, P<0.001). Although no significant difference was observed in recurrence pattern between F0 and F1-3, F4 showed a significantly higher incidence of multiple recurrences (53.3% vs. 23.6%, P<0.01) and recurrence pattern with higher incidence of contralateral (36.7 % vs. 7.3 %) and bilateral (32.2 % vs. 14.5 %) recurrence (P=0.001) than F1–3 during follow-up.
Conclusion: Patients with fibrosis carries a poor oncological prognosis. The oncologic prognosis of HCC can be improved by treatments that inhibit or ameliorate fibrosis.

Workshop 3 [Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD]
WS3-4 10016

Impact of Chemotherapy on Liver

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Introduction: Chemotherapy induced liver injury is one of the common causes of mortality in cancer patient. One of the mechanisms of development of fatty liver is hepatic steatosis induced by chemotherapeutic agents. Here in this study we are evaluating the development of fatty liver during the therapy for ovarian cancer.
Method: A prospective study was conducted on cases of ovarian cancer with normal liver function test, which developed fatty liver after getting chemotherapy.
Result: We studied 200 cases of ovarian cancer, out of which 31 (15%) cases developed fatty liver secondary to therapy for ovarian cancer. The mean value of age that developed fatty liver is 49.2 years. Among various clinical parameters, only weight and body surface area (BSA) did show a statistically significant correlation (p=0.05) with the development of fatty liver. The patients who had PFI more than 15 months also showed the development of FL (P=0.03).
Conclusion: Development of fatty liver following chemotherapy follows the common mechanism, but the process is fast. This may be due to an altered metabolic process. Here also weight and BSA are associated with the development of fatty liver. Following chemotherapy, progression-free interval also has shown a significant correlation with the development of fatty liver.

Workshop 3 [Liver Cirrhosis (Fibrosis) & Its Complications, NASH/ NAFLD]
WS3-5 10145

Big Data Analysis of Fatty Liver, Liver Stiffness and Liver Cancer Frequency within Cancer Center Hospitals

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Purpose: We examined the relationship between liver stiffness and liver fat content distribution and liver cancer by FibroScan.
Methods: We used 4214 FibroScan data (LSM: Liver Stiffness Measurement /CAP: Controlled Attenuation Parameter) and 73634 HBV, HCV data extracted from data warehouse, and 983 HCC data from 26783 cancer registry data of prefectural cancer center hospitals.
Results: LSM>=12.0&CAP>=260, LSM>=12.0&CAP<260, LSM<12.0&CAP>=260, LSM<12.0&CAP<260 were 5.7%, 24.7%, 11.7% and 58.3% of the total, respectively. 4.3%, 28.1%, 9.1% and 58.4% of the HCVAb positive subjects, respectively. 7.3%, 23.4%, 23.0% ,46.3%, and a higher proportion of LSM<12.0&CAP>=260 in HCV negative patients. The HCC incidence rate was 10.0 v.s. 20.3 in the HCVAb-negative patients with LSM>=12.0, CAP>=260and CAP<260, respectively, showing a fatty liver has a lower frequency of cancer than fatty liver with some fibrosis. A similar trend of 4.5% v.s. 18.2% was observed among HCVAb-positive patients.
Conclusion: Crossectional analysis of FibroScan shows that when standardized by fibrosis, higher liver fat content is weakly linked to liver cancer frequency.

Workshop 4 [Basic Science & Pathology]
WS4-1 10118

Immunoglobulin-like Transcript 2 as an Impaired Anti-tumor Cytotoxicity Marker of Natural Killer Cells in Patients with Hepatocellular Carcinoma

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Background: Treatment outcomes of systemic therapies against advanced HCC remain unsatisfactory. Natural killer (NK) cells play a pivotal role in immune surveillance against HCC. We aimed to explore new potential targets for immune intervention by revealing the phenotypes of NK cells in HCC patients.
Methods: We examined peripheral NK cells (pNK) and intrahepatic NK cells in HCC patients, and also pNK obtained from healthy volunteers (HVs). We analyzed 39 surface markers on NK cells by mass cytometry. We cultured NK cells in the presence of K562 cells or Daudi cells to evaluate cytotoxicity and antibody-dependent cellular cytotoxicity (ADCC) activity.
Results: The expression levels of activating NK cell markers decreased with aging, while inhibitory markers increased. The expression levels of ILT2 on CD56dimNK cells were higher, while Siglec-7, DNAM-1, and 2B4 were lower in HCC patients as compared with age-matched HVs. ILT2+CD56dimNK cells were enriched in cancer lesions as compared with non-cancerous lesions. ILT2 on CD56dimNK cells was induced in the presence of HCC via the MIF-CXCR4 axis. ILT2+NKp46-CD56dimNK cells exhibited lesser capacity of cytotoxicity and ADCC compared with ILT2-NKp46-and NKp46+CD56dimNK cells. The function of ILT2+NKp46-CD56dimNK cells was partially restored by the ILT2 blockade.
Conclusion: ILT2+CD56dimNK cells increased in the HCC liver and functionally impaired. ILT2 could be a new therapeutic target in HCC patients.

Workshop 4 [Basic Science & Pathology]
WS4-2 10093

Novel Monoclonal Antibody and ADAM17 Enzymatic Inhibitor could Induce NK Cell-mediated Cytotoxicity in HCC by Targeting NKG2D Ligands

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Background: The net signaling balance between activating and inhibiting pathway of natural killer (NK) receptors determines the ability of NK cell-mediated immunosurveillance. The major NK activating pathway is related to NK group D ligands (NKG2DLs) including MICB. Whereas, accumulation of membrane-bound NKG2DLs (m-NKG2DLs) enhances NK cell cytotoxicity against hepatoma cells, mNKG2DLs cleavage releases soluble NKG2DLs (s-NKG2DLs), which act as immunological decoys in the serum to prevent antitumor activity. Cancer escape from immunosurveillance via mNKG2DLs shedding is mainly accomplished by a disintegrin and metalloproteases (ADAMs). In this research, we investigated the inhibitory potency of MICB shedding by enzymatic ADAM inhibitor and our novel monoclonal antibody, 7C6, targeting MICB shedding portion.
Methods: Human HCC cell line PLC/PRF/5 and HepG2 cells were treated with 7C6. S-MICB and m-MICB levels were measured by an ELISA kit and FACS, respectively. In the knockdown of notable active ADAMs in human, the specific siRNAs of each were used. We further screened potential ADAM inhibitor by using FDA-approved drugs in vitro.
Results: Knockdown of ADAM17 significantly inhibited MICB shedding. To the importance, lomofungin, an antifungal drug, was found to strongly decrease ADAM17 activity. Furthermore, lomofungin and 7C6 decreased s-MICB and increased m-MICB in a dose-dependent manner. These effects by lomofungin were cancelled upon ADAM17 knockdown, suggesting that lomofungin targeted ADAM17.
Conclusion: This result suggests lomofungin could be an attractive agent for the immunological control of HCC to target the modulation of NKG2DLs via the suppression of ADAM17. Furthermore, 7C6 also inhibited MICB shedding to potentially induce stronger NK cell-mediated cytotoxicity.

Workshop 4 [Basic Science & Pathology]
WS4-3 10100

Fibroblast Growth Factor Inhibition by Molecular-targeted Agents Mitigates Immuno-suppressive Tissue Microenvironment in Hepatocellular Carcinoma

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Background: Combination immunotherapy, immune checkpoint inhibitors plus molecular-targeted agents (MTAs) have been approved for the treatment of advanced hepatocellular carcinoma (HCC). This study aimed to investigate the impact of MTAs on the tumor immune microenvironment (TIME).
Methods: We established immune syngeneic orthotopic HCC mouse models using Hep-55.1C and Hep-53.4, and treated them with MTAs (lenvatinib, sorafenib, regorafenib, cabozantinib, and DC101 as anti-VEGFR-2 antibody, and AZD4547 as FGFR-1/2/3/4 inhibitor) for 2 weeks. To evaluate the alterations in the TIME caused by MTAs, we performed an immunohistochemical assessment (antibodies for CD3, CD8, Foxp3, GrB, Arginase-1, NK1.1, F4/80, CD11c, PD-1, and PD-L1). We conducted RNA-seq analysis using lenvatinib- and AZD4547-treated tumors. To confirm the clinical relevance of these findings, we analyzed the RNA-seq data of human HCC cells treated with lenvatinib for 24 h using the Gene Expression Omnibus database.
Results: The number of Foxp3- and F4/80-positive cells decreased in many MTAs. Cabozantinib increased the numbers in NK1.1-, GrB, and CD11c-positive cells. Lenvatinib and AZD4547 increased the number of CD8-, GrB-, and PD-L1-positive cells. Gene ontology enrichment analysis revealed that lenvatinib and AZD4547 commonly downregulated lipid metabolism-related genes. In human HCC cells, 161 genes downregulated by FGFR inhibition in mouse models overlapped with those downregulated by lenvatinib.
Conclusions: We showed (1) cabozantinib activated the innate immune system and (2) lenvatinib and AZD4547, which inhibit FGFR signaling, altered TIME to a hot immune state by downregulating lipid metabolism-related genes. These findings may contribute to clarifying the mechanisms of combination immunotherapies on TIME of HCC.

Workshop 4 [Basic Science & Pathology]
WS4-4 10099

Prevention of Liver Carcinogenesis by Glycine in Hepatocyte-specific PTEN Knockout Mice

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Background: We have previously shown that the amino acid glycine ameliorates steatohepatitis in animal models. Here we investigated the effect of glycine on steatohepatitis-related liver carcinogenesis using hepatocyte-specific phosphatase and tensin homolog deleted from chromosome 10 (PTEN)-knockout mice.
Methods: Male Alb-Cre TG (+) PTENflox/flox mice (PTEN KO) aged 11-17 weeks were fed a normal diet or a diet containing 5% glycine for 2 or 24 weeks. Wild-type or TG (-) mice fed a normal diet were used as control. The expressions of 4-hydroxynonenal (4HNE) and CD8 in liver were stained by immunohistochemistry. The expression of mRNA in liver tissue was measured by RT-PCR.
Results: PTEN KO developed severe steatohepatitis, whereas glycine-containing diet for 2 weeks improved steatohepatitis and significantly decreased serum AST and ALT levels. After 24 weeks, PTEN KO developed 2.6 ± 1.0 liver tumors ($\varphi > 2$ mm), while glycine completely suppressed tumorigenesis to 0 ± 0. The expression of IL12b mRNA in liver tissue of PTEN KO was increased more than 5 times by glycine diet than normal diet. Similarly, the expression of interferon γ was significantly increased in PTEN KO fed glycine compared to the normal diet group. CD8-positive cells in liver tissue were markedly increased in PTEN KO fed glycine, suggesting that antitumor immunity was enhanced in the liver of PTEN KO fed with glycine.
Conclusion: Glycine-containing diet ameliorated steatohepatitis and prevented hepatocarcinogenesis by enhancement of antitumor immunity in hepatocyte-specific PTEN knockout mice. It is expected that glycine contributes to prevention of NASH-related HCC.

Workshop 4 [Basic Science & Pathology]
WS4-5 10114

Role of ZHX Family Proteins in Hepatocarcinogenesis Studied by Immunohistochemical Staining

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Background: Transcription factors (TFs) play an important role in regulating gene expression through a complex network system. Many TFs, such as the zinc fingers and homeobox (ZHX) family, act as both tumor inducers and suppressors. We investigated the relationship between nuclear and cytoplasmic expression levels of ZHX TFs in four pathological liver tissues and hepatocellular carcinoma (HCC).
Methods: Immunohistochemical staining was performed in 33 pairs of HCCs and adjacent tissues to detect the expression levels of ZHX-1, -2 and -3 proteins. Next-generation sequencing (NGS) and digital PCR (dPCR) were also deployed to investigate somatic mutations in these HCCs and their relationship with ZHX expression and clinicopathological features.
Results: ZHX-1 expression in HCC was significantly stronger in both cytoplasm and nuclei compared to adjacent tissues (p&lt0.01). In contrast, for ZHX-2, expression was stronger in the nucleus in HCC compared to adjacent tissues (p&lt0.05), but no obvious difference in the cytoplasm; for ZHX-3, there was no obvious difference in expression in the nucleus but lower in the cytoplasm (p&lt0.05). HCC with high ZHX-1 and ZHX-2 expression in the nucleus and cytoplasm were significantly associated with unfavorable OS while HCCs with high ZHX-3 expression in the cytoplasm was significantly associated with favorable OS (p=0.013). High ZHX-1 expression in the cytoplasm of HCC was associated with low TERT mutation frequency and high infection rate of hepatitis B virus.
Conclusion: ZHX1-3 proteins are expressed in HCCs, but the different expression patterns for each protein suggest that each ZHX protein plays a different role in hepatocarcinogenesis.

Workshop 5 [Basic Science & Pathology 2]
WS5-1 10045

Intrahepatic IgA Complex Induces Polarization of Cancer Associated Fibroblasts into the Matrix Phenotype in the Tumor Microenvironment of HCC

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Background: Cancer associated fibroblasts(CAFs) are a group of activated fibroblasts and play a key role in the tumor microenvironment(TME). Immunoglobulin A(IgA) usually neutralizes pathogens against infections at the mucosal sites. IgA has also been reported to contribute to inflammation or dismantling antitumor immunity in human liver. we investigated the effects of IgA complex on CAFs in TME of HCC.
Methods: The dynamics of CAFs in the TME of HCC were analyzed using single-cell RNA sequencing in three HCC samples. CAFs were isolated from thirty HCC samples. Isolated CAFs were treated with mock or serum-derived IgA dimer. CD71 and PD-L1 expression levels in CAFs were analyzed by flow cytometry.
Results: We identified five CAF subtypes in the TME of HCC. In a patient with high IgA serum, the sub-cluster proportions in matrix CAF-FAP were increased. We performed flow cytometry on fresh surgical tissues and observed an increase in the MFI of FAP($p=0.001$) in CD68+cells from patients with high serum IgA(n=14) compared to those with low serum IgA(n=8). Furthermore, we observed an increase in the MFI values of CD71 and PD-L1($p<0.05$) in the FAP+CAF from the high IgA group compared to the low IgA group. We have confirmed that the transferrin receptor(CD71) is expressed in CAFs. IgA-treated CAFs showed increased PD-L1 MFI values compared with mock-treated CAF.
Conclusions: The correlation between IgA cpmplex and matrix CAFs may contribute to the establishment of immunosuppressive TME and poor prognosis of patients. Targeting this CAF subtypes may overcome the resistance of Immune checkpoint blockade therapy.

Workshop 5 [Basic Science & Pathology 2]
WS5-2 10026

The Role and Mechanism of LincRNA Encoded Peptide in the Progression of Hepatocellular Carcinoma

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At present, a large proportion of advanced hepatocellular carcinoma (HCC) patients are unable to benefit from immune checkpoint inhibitors or targeted therapies, so developing novel therapeutic drugs for HCC is of great importance. Recently, there was number of peptide was identified that encoded by lincRNA and participate in the progression of cancer. Through multiomic screening and verification, we identified SMIM45 was encoded by LINC00634 and was a small endogenous peptide. Our results showed that SMIM45 protein level was high in HCC tissues compared to adjacent tissues and SMIM45 could promote HCC cell proliferation and cell migration. Moreover, we further confirmed that SMIM45 interacted with MTDH by immunoprecipitation, and found that the protein level of MTDH was increased with SMIM45 overexpression, but not vice versa. The literatures indicated that MTDH could be degraded by ubiquitination though interacting with ubiquitin E3, and molecular docking showed that ubiquitinated MTDH affected the interaction with SMIM45. Therefore, we hypothesized that SMIM45 could interact with MTDH to promote HCC development by inhibiting ubiquitination of MTDH. Finally, conclude that SMIM45 binds MTDH, causing reduced ubiquitination of MTDH and promoted HCC progression. The work will provide a new biomarker for HCC and a new target for HCC cancer therapy.

Workshop 5 [Basic Science & Pathology 2]
WS5-3 10067

Interaction between HSC and LSEC Populations in the Premalignant Environment of DEN-Treated Cytoglobin Knock-out Mice

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Background: Cytoglobin (Cygb), the fourth member of globin family in mammals, possesses the antioxidant function via scavenger reactive oxygen species. Here we examine how Cygb can protect mice from liver tumor formation.
Method: Cygb deficient (Cygb-KO), Cygb overexpressing (Cygb-TG) or wild-type (WT) mice (n = 10-20 each group) were administrated with Diethylnitrosamine (DEN). Serum and liver tissues were collected for molecular analysis. Primary non-parenchyma cells were isolated from DEN-treated livers for single-cell RNA sequencing (scRNA-seq) by 10X Genomics.
Result: High dose of DEN, 25 ppm in drinking water for 25 weeks, induced 100% liver, and 40% lung tumors in KO mice, but only 40% and 0%, respectively, in WT mice. When mice were injected with 6 μg/g BW of DEN at 15 days old, the mean number of liver tumors in WT was 4.76 compared to 1.51 in Cygb-TG, $p<0.001$; and the maximum size of liver tumors was 7.4 mm in WT compared to 2.05 in Cygb-TG mice, $p<0.01$. Cell annotation in scRNA-seq of DEN-treated livers from KO, WT revealed 24, and 19 clusters of cells, respectively. Integrated data have been found 5 sub-clusters of LSECs and 3 of HSCs. The number of HSCs in the premalignant area of KO mice is significantly higher compared to WT one. NicheNet pipeline analysis of cell-cell interaction has identified the significantly higher activity of ligand-receptors interacting pattern between HSCs or immune cells with LSEC.
Conclusion: Cygb may regulate tumor formation in mice via mediating cell-cell interaction.

Workshop 5 [Basic Science & Pathology 2]
WS5-4 10041

Anti-proliferative Effects of a Flavonoid from Anomianthus Dulcis Sincl. on Hepatocellular Carcinoma

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Background: Liver cancer, hepatocellular carcinoma (HCC), and cholangiocarcinoma (CCA), is the most prevalent cancer among Thai male, with the highest mortality caused by cancer. Anomianthus dulcis Sincl. has been used in Thai traditional medicine in various therapeutic indications. However, the effects on liver cancer treatment have not been elucidated.
Methods: Dry flowers of A. dulcis were extracted using organic solvents, and the chemical constituents were purified by chromatographic methods. The chemical structures of the pure compounds were elucidated using spectroscopic techniques and compared with the reported literature. Cytotoxicity on HCC cells was examined using SRB assay, and the effects on cell proliferation were determined using flow cytometry. The mechanisms underlying HCC inhibition were examined by Western blot.
Results: Among 4 purified flavonoids; pinocembrin, pinostrobin, chrystin, 3-farnesylindole, only pinocembrin showed an inhibitory effect on the proliferation of two HCC cell lines; HepG2 and Li-7, whereas chrystin showed specific toxicity to only HepG2. Pinocembrin was then selected for further study on the underlying mechanisms. Flow cytometric analyses revealed that pinocembrin arrested the HCC cell cycle at the G1 phase with a minimal effect on apoptosis induction. Pinocembrin exerted the suppression of the STAT3 signaling pathway in HCC cells and thus inhibited the expression of cell cycle regulatory proteins, namely cyclin D1, cyclin E, and CDK6, and reduced the phosphorylation of retinoblastoma proteins.
Conclusion: Pinocembrin extracted from A. dulcis exerted a significant growth inhibition on HCC cells via suppressing STAT3 signaling pathways and its downstream-regulated genes.

Protective Effect of Ischemic Preconditioning on Hepatic Ischemia-reperfusion Injury in Rats

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Aim: Ischemic preconditioning (IPC) protects tissue against ischemia and reperfusion (I/R) injury. The aim of this study was to examine the impact of IPC on protection of hepatocytes after prolonged I/R injury.
Methods: Twenty four Wistar rats were randomly divided into ischemic preconditioning group (IP), ischemia/ reperfusion group (IR) and sham operation group (SO). A model of partial liver ischemia/reperfusion was used, in which rats were subjected to liver ischemia for 90 min prior to reperfusion. The animals in the IP group underwent ischemic preconditioning for 10 min prior to the ischemia/reperfusion challenge. After 3h of reperfusion, serum and liver tissue in each group were collected to detect the level of serum ALT, AST, HA, MDA and liver histopathology.
Results: Compared with IR group, IP group showed a significantly lower ALT, AST, HA and MDA level in 3h. Proliferation index (PI) was significantly increased in IP group compared with IR group.
Conclusion: Ischemic preconditioning can protect liver cells against ischemia/reperfusion injury, which may be related to cell proliferation during early ischemic reperfusion.

Workshop 6 [Basic Science & Pathology 3]
WS6-1 10068

Enhancing Tumor Immunogenicity of Hepatocellular Carcinoma Using a Novel Cancer Vaccine

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Background: The efficacy of Immune checkpoint inhibitor against hepatocellular carcinoma (HCC) is still limited around 20% due to low tumor immunogenicity, referred to as Cold HCC. We have developed a novel cancer vaccine that composed of heat shock protein 70 (HSP70) and Glypican-3 (GPC3)-derived peptides with two adjuvants (hLAG-3Ig and Poly-ICLC). We have finished Phase I trial using this vaccine perioperatively against resectable HCC. Here we'll present the results of the immunological analysis of the tumor microenvironment.
Method: 20 HCC patients received six preoperative vaccine doses, followed by radical resection. An additional 20 HCC patients who underwent resection without vaccination were analyzed as control group. Immunohistochemistry (IHC) and mass cytometry (CyTOF) were performed to conduct immunological analyses of the resected specimens.
Results: IHC analysis revealed high infiltration of CD8+ T cells in 12 of 20 patients within the vaccine group and in 7 of 20 patients in the control group. CyTOF analysis demonstrated that the presence of activated tumor-antigen specific (CD107a+ CD39+ PD-1+ TIM3-) CD8+ T cells with diminished immunosuppressive regulatory T cells were only observed in the vaccination group. Moreover, nearest neighborhood analysis using multicolor IHC analysis suggested the relationship between activation of CD8+ T cells and Treg cells.
Conclusion: This vaccine therapy has the potential to induce activated tumor antigen-specific T cells into HCC and may partially convert cold HCC to hot HCC.

Workshop 6 [Basic Science & Pathology 3]
WS6-2 10038

High-grade Nuclear Atypia is an Unfavorable Factor for Postoperative Recurrence of Hepatocellular Carcinoma

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Aim: We created a deep learning model to quantify nuclear atypia of hepatocellular carcinoma (HCC) from liver specimens and investigated relationship between nuclear atypia and recurrence after surgical resection in HCC.
Methods: Seventy-eight patients who were underwent curative surgical resection for HCC were included. We created deep learning models to quantify nuclear atypia using whole slide images of liver specimens and HALO AI software.Nuclei with 1.5 times larger than those of non-tumor hepatocytes and with multinuclei or irregular shape nuclei were annotated as High-grade nuclear atypia (HGA). In this model, the HGA ratio (percentage of HGA area) was quantified. In addition, nuclear atypia was semiquantitatively evaluated by two pathologists under the microscope (G1: nucleus size equivalent to that of non-tumor hepatocytes, G2: nuclei other than G1/G3, G3: large nuclei with obvious morphological irregularities).
Results: Microscopic nuclear atypia in the 78 HCC tissues included 23 cases of G1, 28 cases of G2, and 27 cases of G3. The HGA rate of G3 cases was significantly higher than that of G1 or G2 cases (G3 vs G1, $p=0.01$; G3 vs G2, $p<0.01$). When the median HGA rate was used to divide the HGA into high grade (HG) and non-HG groups, the HG group had more poorly differentiated HCC ($p<0.01$), higher Ki-67 labeling index ($p<0.01$), more frequent portal vein invasion ($p=0.02$), and lower postoperative recurrence-free rate ($p=0.02$) than the non-HG group.
Conclusions: Quantitative evaluation of nuclear atypia in HCC may be useful to identify HCC with high recurrence rate.

Workshop 6 [Basic Science & Pathology 3]
WS6-3 10017

Findings of Liver Pathology in Autopsy

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Introduction: Lesions of liver cause significant morbidity and mortality even without causing significant sign & symptom. Liver biopsy may not give the exact picture. Autopsy study may be a better choice.
Material and Method: Retrospective analysis of histopathological findings of autopsy cases was done during year 2017 -20. Only those cases were selected, which showed positive histopathological finding in heart, lung, liver, spleen, kidney and brain. Total 70 cases were taken. The age group was between 4 days to 77 years. Male and female were 52 and 18 respectively. Out of total 70 cases, 41 showed significant lesions in liver, which were analyzed.
Result: Most common lesion was moderate to severe degree of Hepatic steatosis which showed foci of cirrhosis 14/70 (20%). Grossly most of the cases were mixed type of cirrhosis; macronodular & micronodular. Next prominent group of diseases were cirrhosis (9/70)12.8%. Other common diseases were chronic hepatitis & granuloma 4/70 (5.7%) each. Cardiac cirrhosis was seen in 2/70 cases, which was confirmed by finding fibrosis in myocardium. Nonalcoholic hepatic steatosis was seen a case of 11 months old male baby who presented with umbilical granuloma on gross examination and lung also showed pneumonic features. Other conditions were hydatid cyst, metastasis from primary cancer of unknown origin and Acute inflammatory cell infiltration in chronic hepatitis were seen in 1/70 cases.
Conclusion: Histopathological examination of Post mortem specimens is conducted at limited centers in our country. This diminishes opportunity of medical professionals to learn about liver pathology.

Workshop 6 [Basic Science & Pathology 3]
WS6-4 10029

Significance of Partial Portal Arterialization in Small Bowel Transplantation for the Liver

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Aim: Bowel transplantation has proved feasible in man, but several important questions have yet to be answered. One consideration is the site of venous outflow of the allograft. Portal drainage, however, re-establishes the physiological route of venous outflow, while systemic drainage creates a partial mesocaval shunt.
Methods: We used canine models. 1.portacaval shunt <Eck.n=6 >2. intestinal autotransplantation with systemic venous outflow ,< MCA. n=5 >. 3. intestinal autotransplantation with systemic venous outflow plus partial arterialization, spleno-spleno AV fistel, &lt MCA+A, n=5 >. Sham ope, n=5. Postoperative 4 weeks after, we calculate hepatic blood flow, amino acid, NH3, and hepatic ATP.
Results: The metabolic changes observed after MCA did not parallel the changes, hyperammonia and amino acid imbalance seen after Eck. Hepatic ATP in MCA was significantly lower values than control. But hepatic ATP in MCA+A was similar to control.
Conclusion: This experimental study showed that partial portal arterializations has beneficial effects on liver under Intestinal autotransplantation with systemic venous outflow.

Workshop 7 [Systemic Chemotherapy & Oncology 3]
WS7-1 10129

A Prospective Study to Assess the Safety and Efficacy of Ramucirumab in Advanced Hepatocellular Carcinoma Patients in Japanese Real-world Practice: R-evolution Study

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Background: The purpose of this study is to complement the results of the REACH-2 study by prospectively evaluating the safety and efficacy of ramucirumab for advanced hepatocellular carcinoma (aHCC) in real-world settings.
Methods: This was an open-label, non-randomized, multicenter, prospective study conducted at 13 institutions in Japan (jRCTs031190236). The study included Child-Pugh A patients with aHCC who had received pretreatment with lenvatinib or atezolizumab plus bevacizumab (Atezo/Bev). Ramucirumab was introduced as a second-line treatment after lenvatinib or Atezo/Bev, and as a third-line treatment after Atezo/Bev and lenvatinib. Prior to the study, 7 patients had received treatment with lenvatinib, 7 patients with Atezo/Bev, and 3 patients with Atezo/Bev followed by lenvatinib.
Results: Between May 2020 and July 2022, a total of 19 patients were enrolled in the study. Of these, 17 patients received ramucirumab and were included in the analysis. The median PFS and OS were 3.7 and 12.0 months, respectively. The most frequent grade 3 or higher adverse events (AEs) were hypertension (23.5%), proteinuria (17.6%), and neutropenia (11.8%). The discontinuation rate due to AEs was 35.3%. Six patients transitioned from Child-Pugh A to B after ramucirumab treatment. Thirteen patients were able to receive posttreatment after ramucirumab, including systemic chemotherapy in 10 patients, hepatic arterial infusion chemotherapy in 2 patients, and radiotherapy in 1 patient.
Conclusions: Ramucirumab activity was observed when used after lenvatinib and Atezo/Bev. However, the incidence of AEs was higher than in the REACH-2 trial. Further study is warranted to confirm the potential of ramucirumab in these settings.

Workshop 7 [Systemic Chemotherapy & Oncology 3]
WS7-2 10104

A Randomized Phase II Trial to Assess Safety and Efficacy of Regorafenib in Patients with Advanced Hepatocellular Carcinoma who were not Included in the RESORCE Trial: REGAIN Trial

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Background: Regorafenib was approved as a second-line treatment for hepatocellular carcinoma based on the RESORCE trial. In the REORCE trial, patients who tolerated sorafenib (SOR) (>=400 mg/day for >=20 of last 28 days of treatment) were enrolled. In clinical practice, SOR is often reduced to lower dose due to various adverse events (AEs). Furthermore, evidence is lacking on regorafenib after atezolizumab+bevacizumab (Atezo/Bev) and lenvatinib (LEN).
Methods: This study was a randomized control, open-label phase II trial (jRCTs031190103). This trial consists of three arms (post-SOR arm: SOR 200 mg/day or 400 mg/every other day as prior therapy; post- LEN arm: lenvatinib as prior therapy; post-Atezo/Bev arm: Atezo/Bev as prior therapy). In each arm, patients were assigned to a usual dose group (160 mg/day) or a dose-reduction group (80 mg/day) of regorafenib to evaluate safety and efficacy of different starting doses. The primary endpoint was time to progression (TTP). The secondary endpoints of safety were incidence of AEs and discontinuation rate due to AEs.
Results: Twelve patients were enrolled in each arm and total of 36 patients started regorafenib. Discontinuation by AEs within 4 weeks was observed in 1 out of 36 patients (2.8%). In the whole study period, discontinuation rate due to AEs was 17.6% in the usual dose group and 25.0% in the dose-reduction group. The median TTP was 4.6 months in the usual dose group and 3.0 months in the dose-reduction group.
Conclusions: The results demonstrated that regorafenib can be a therapeutic option for second-line treatment in these settings.

Workshop 7 [Systemic Chemotherapy & Oncology 3]
WS7-3 10056

Efficacy of Lenvatinib Combined with Transcatheter Intraarterial Therapies for Patients with Advanced-stage of Hepatocellular Carcinoma: A Propensity Score Matching

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Aim: To evaluate the effect of lenvatinib (LEN) combined with transcatheter intra-arterial therapy (TIT) in patients with advanced-stage hepatocellular carcinoma (HCC) after propensity score matching (PSM).
Methods: We retrospectively enrolled 115 patients with advanced-stage HCC who received LEN treatment. The patients were categorized into the LEN combined with TIT group (n=30) or the LEN monotherapy group (n=85). After PSM, 38 patients (LEN + TIT group, n=19; LEN monotherapy group, n=19) were analyzed.
Results: The median overall survival (OS) in the LEN + TIT group was significantly higher than that in the LEN monotherapy group (median survival time (MST); 28.1 months vs. 11.6 months, p = 0.014). In the sub-group analysis, the median OS in the LEN combined with transcatheter arterial chemoembolization and LEN combined with hepatic arterial infusion chemotherapy groups was significantly higher than that in the LEN monotherapy group (MST 20.0 vs. 11.6 months, 30.2 vs. 11.6 months, p = 0.048, and p = 0.029, respectively). The independent factors associated with OS were alpha-fetoprotein and LEN combined with TIT in the Cox regression analysis. The indications for LEN combined with TIT were aged less than 75 years and modified albumin bilirubin(m-ALBI) grade 1.
Conclusion: LEN combined with TIT improved prognosis compared with LEN monotherapy in patients with advanced-stage HCC after PSM. Moreover, the intervention with LEN combined with TIT is recommended for a population aged less than 75 years and with m-ALBI grade 1.

Workshop 7 [Systemic Chemotherapy & Oncology 3]
WS7-4 10134

The Effectiveness of Durvalumab plus Tremelimumab Treatment for Hepatocellular Carcinoma after Treatment with Anti-VEGF Drugs

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Background: Durvalumab plus tremelimumab (DUR/TRE) is a new first-line treatment in combination with immune checkpoint inhibitors for hepatocellular carcinoma (HCC) that is available worldwide. We evaluated the efficacy and safety of DUR/TRE for treating HCC.
Methods: This study population included ten patients we could follow from 14 patients who received DUR/TRE treatment in our hospital between April 2023 and June 2023. We evaluated the DUR/TRE treatment profile, clinical response (according to RECIST), adverse events (according to CTCAE v.5.0), and progression-free survival (PFS).
Results: The study population included 9 male patients. The ECOG performance status (PS) of all patients was classified as zero. Seven patients had BCLC stage B, and 3 patients had C. The modified ALBI grades were as follows: 1 (n=2), 2a (n=5), and 2b (n=3). The reasons for performing DUR/TRE treatment included systemic therapy naivety (30%), and progressive disease after atezolizumab plus bevacizumab [ATZ/BEV] (50%). The tumor responses were classified as follows: disease control rate (DCR), 20.0%; and PFS, 1.95 months (95% CI 0.65-2.89). There were no significant differences in either DCR or PFS between the systemic therapy-naïve patients and the other patients (p=0.478 and p=0.699, respectively). One patient who received DUR/TRE treatment after ATZ/BEV treatment achieved a PR. The rates of AE (any grade/grade ≥3) were as follows: colitis (20/10%), dermatitis (20/0%).
Conclusions: DUR/TRE treatment is effective for HCC, even in patients who received ATZ/BEV treatment; however, it is very important to pay attention to specific immune-related AEs that are different from previous systemic treatments for HCC.

Early Experience of Durvalumab plus Tremelimumab in Patients with Unresectable Hepatocellular Carcinoma

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Background: Durvalumab plus tremelimumab (Dur+Tre) for patients with unresectable HCC has been used since April 2023 in Japan. We investigated the efficacy and safety in an early phase after the administration of Dur+Tre.
Methods: A total of 20 patients who received Dur+Tre at our institution from April 2023 were enrolled. The radiological evaluation was performed using RECIST v1.1. Adverse events (AEs) were evaluated according to the CTCAE ver5.0.
Results: The median age of the patients was 75 (50-91) years. The median ALBI score was -2.03, and 65% of the patients were modified ALBI grade 2b. Line of treatment was 1st (n=1), 2nd (n=4), 3rd (n=4), 4th (n=3), 5th (n=5), and 6th-line (n=3). Fifteen (75%) patients were BCLC stage C, and 5 patients were BCLC stage B. The radiological assessment was performed on 9 patients. Objective response in 1st ~3rd-line patients (n=4) was 50%, and 20 % in 4th and later-line patients (n=5). Disease control rate in 1st ~3rd-line patients was 75%, and 20% in 1st ~3rd-line patients. AFP decrease after 4W was observed in 6 of 19 patients. Grade 3 irAEs were reported in 7 patients (colitis, renal dysfunction, and adrenal insufficiency). Three of 4 patients with immune-related colitis received infliximab as steroid-refractory immune-related colitis, and all three patients showed good prognosis.
Conclusion: AFP decrease after 4 weeks from the administration of durvalumab plus tremelimumab was observed in 31.6% of patients. The differences in efficacy and safety between early and late-line patients should be discussed in further prospective studies.

Workshop 8 [Systemic Chemotherapy & Oncology 4]
WS8-1 10015

Survival Improvements in Advanced Hepatocellular Carcinoma with Systemic Therapy Over the Past Decade

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Aim: Over the past decade, treatment modalities for advanced hepatocellular carcinoma (HCC) have changed dramatically with systemic therapy as the primary option. However, the effect of sequential treatment on the prognosis remains unclear.
Methods: This retrospective study included patients who began systemic therapy between 2009 and 2022. Patients were separated into three groups according to the initial date of systemic therapy. Patient characteristics including number of therapy lines, treatment efficacy, and overall survival (OS) were compared. Multivariate analyses of the prognostic factors were analyzed using the Cox proportional hazards model.
Results: A total of 349 patients were included (period 1: 2009-2013, n=86; period 2: 2014-2018, n=139; period 3: 2019-2022, n=124). A significant trend in etiology was observed with decreasing viral hepatitis-related HCC and increasing non-viral hepatitis-related HCC. The proportion of patients who were administered more than two lines eventually increased (1.2%, 12.2%, and 18.6% in period 1, 2, and 3, respectively; p<0.001) and the median OS was significantly prolonged (14.3, 17.2, and 30.0 months in period 1, 2, and 3; p<0.001). Use of less than three lines, non-complete and partial response of a first-line, modified albumin-bilirubin grade 2b or 3, intrahepatic tumor number >=5, presence of extrahepatic metastasis and alpha-fetoprotein value >=400 ng/ml were identified as the strongest factors for a shorter OS.
Conclusions: Over the past decade, the availability of sequential therapies has contributed to significant improvements in the prognosis of patients with HCC. Sequential treatment post-progression is valuable for prolonging survival.

Workshop 8 [Systemic Chemotherapy & Oncology 4]
WS8-2 10003

Association between Presarcopenia and Clinical Outcomes in Patients with Advanced Hepatocellular Carcinoma Undergoing Systemic Therapy: A Comprehensive Study and Meta-Analysis

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Background: This systematic review and meta-analysis aimed to assess the prevalence and impact of presarcopenia in patients undergoing systemic therapy for advanced hepatocellular carcinoma (aHCC).
Methods: We searched the MEDLINE and Embase databases until November 2022 to investigate the association between presarcopenia and overall survival (OS) or progression-free survival (PFS) of aHCC patients receiving systemic therapy. The included studies were retrospective cohort studies that evaluated the muscle index of the third lumbar spine using CT images. The Newcastle-Ottawa scale was applied to assess the quality of the included studies. The study outcomes were the prevalence of presarcopenia and its associations with OS and/or PFS, presented as a pooled hazard ratio (HR) with a 95% confidence interval (CI). Subgroup analysis and sensitivity analysis were performed. Publication bias was evaluated with a funnel plot and the Egger test.
Results: A total of 19 studies comprising 2,280 patients were included. The pooled prevalence of presarcopenia was 43.2% (36.3-50.4%). Presarcopenia was associated with poor OS with an HR of 1.70 (95%CI:1.46-1.97; p<0.001) and a decreased PFS (HR:1.29, 1.12-1.48; p<0.001). The association between presarcopenia and reduced OS was observed in subgroup analyses of sorafenib treatments (1.74, 1.41-2.14; p<0.001), lenvatinib (1.71,1.22-2.41; p=0.002) and immunotherapy (1.61, 1.15-2.24; p= 0.005). The link between presarcopenia and poor PFS was also observed in the subgroup analyses of sorafenib (1.23, 1.03-1.46; p=0.020), lenvatinib (2.08,1.18-3.67; p=0.012) and immunotherapy (1.30, 1.00-1.69; p=0.049).
Conclusions: Presarcopenia is prevalent in aHCC patients undergoing systemic therapy and can predict OS and PFS in this population.

Workshop 8 [Systemic Chemotherapy & Oncology 4]
WS8-3 10006

Consistent Efficacy of Hepatic Artery Infusion Chemotherapy Irrespective of PD-L1 Positivity in Unresectable Hepatocellular Carcinoma

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Background: Atezolizumab/bevacizumab is the first-line chemotherapy for unresectable hepatocellular carcinoma (HCC) patients. In our institute, if the patient is not feasible for or cannot afford the first-line systemic chemotherapy, hepatic artery infusion chemotherapy (HAIC) is proposed and used for treatment The purpose of the study was to determine the correlation, if at all existent, between the PD-L1 positivity of the host's tumor microenvironment and the response to hepatic artery infusion chemotherapy.
Methods: We retrospectively assessed 34 HCC patients who were treated with HAIC and had available biopsy samples between January 2020 and May 2022. We evaluated tumor response, progression free survival (PFS), disease control rate (DCR) and overall survival (OS). Biopsy samples' tumor microenvironments were examined for PD-L1 positivity using combined positivity score (CPS).
Results: There was no difference in OS between HCC patients who had PD-L1 positivity and those who did not. There was no significant difference in PFS and disease control rate (DCR) between HCC patients who had PD-L1 positivity and those who did not. (P value = 0.4584, 0.7763 respectively). In addition, we examined the response rates of advanced HCC patients who were treated with HAIC after atezolizumab/bevacizumab combination therapy (n=12). 50% of patients who were treated with HAIC after atezolizumab/bevacizumab combination therapy showed objective response.
Conclusion: In this report, we confirmed consistent efficacy of HAIC irrespective of PD-L1 positivity and that HAIC may be an option to atezolizumab/bevacizumab progressors.

Workshop 8 [Systemic Chemotherapy & Oncology 4]
WS8-4 10032

Genetic Discrimination between MC and IM could be Useful in Planning Tumor-specific Treatment Strategies for Recurrent Hepatocellular Carcinoma

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The distinction between multicentric occurrence (MC) and intrahepatic metastasis (IM) in recurrent hepatocellular carcinoma has a significant impact on tumor biology and may influence the prognosis. In this study, we genetically compared the primary and recurrent nodules (MC/IM) and tracked the prognosis after resection, aiming to explore tumor-specific recurrent treatment strategies.
Methods: We created an in-house panel covering 72 genes associated with HCC-related mutations and performed genomic analysis using next-generation sequencing for 117 cases of liver resection in our hospital, involving 205 lesions. Among the 117 cases, we performed genetic discrimination (MC/IM) between the primary and recurrent nodules in 25 cases that underwent liver resection for recurrent lesions, and subsequently tracked their prognosis.
Results: Among the 25 cases that underwent resection for recurrent lesions after initial treatment, there were 14 cases of MC recurrence and 11 cases of IM recurrence. There was no significant difference in recurrence-free survival (RFS) between MC and IM recurrence after initial liver resection. However, overall survival (OS) was significantly better in the MC recurrence group (P = 0.015), with 10 out of 14 cases maintaining a relatively long-term tumor-free state after re-resection. On the other hand, among the 11 cases of IM recurrence, 9 cases experienced repeated recurrence after liver resection.
Discussion: Aggressive therapeutic interventions, including resection, can be expected to improve the prognosis after MC recurrent HCC. However, in IM recurrent HCC, even if resection is feasible, the prognosis afterward is relatively poor, and repeating resections without considering tumor-specific factors poses problems.

Abdominal Pain Accompanied by Elevated Serum Inflammatory Markers and Biliary Enzymes for Diagnosing Immune Checkpoint Inhibitor-induced Sclerosing Cholangitis

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Background: Immune-related sclerosing cholangitis (irSC) is relatively rare and its clinical characteristics are not well known. In this study, we aimed to summarize the clinical features of irSC.
Methods: Clinical data were collected retrospectively from 1,393 patients with advanced malignancy treated with immune-checkpoint inhibitors (ICIs) between August 2014 and October 2021. We analyzed patients with immune-related adverse events of liver injury (liver-irAEs) and compared irSC and non-irSC groups.
Results: Sixty-seven patients (4.8%) had a liver-irAE (greater than or equal to Grade 3) during the follow-up period (median, 262 days). Among these, irSC was observed in eight patients (11.9%). All patients in the irSC group were treated with anti-PD-1/PD-L1 antibodies. Compared with the non-irSC group, the irSC group showed mainly non-hepatocellular liver injury (87.5 % vs 50.8 %, P = 0.065), and had elevated serum inflammatory markers (e.g., CRP and NLR) and biliary enzymes (e.g., GGTP and ALP) at the onset of liver-irAEs. Furthermore, most patients with irSC had abdominal pain. In the non-irSC group, the liver injury of 23 patients improved only with the discontinuation of ICIs, and 22 patients improved with medication including prednisolone (PSL). Conversely, almost all patients (n=7) in the irSC group were treated with PSL, but only two patients experienced an improvement in liver injury.
Conclusion: We found that irSC is characterized by a non-hepatocellular type of liver injury with abdominal pain and a high inflammatory response and is refractory to treatment. Further examination by imaging is recommended to detect intractable irSC in cases with these characteristics.

Workshop 9 [Hepatitis C, Hepatitis B]
WS9-1 10115

Usefulness of FIB-4 Index and ALT at 1 Year of Nucleos(t)ide Analog Treatment for Prediction of Hepatocellular Carcinoma in Chronic Hepatitis B Patients

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Background: Patients with chronic hepatitis B virus (HBV) infection are at risk of developing hepatocellular carcinoma (HCC). The aim of this study was to evaluate the dynamics of a non-invasive marker of liver fibrosis, the FIB-4 index, for predicting the development of HCC.
Methods: Among a total of 882 chronically HBV-infected patients who were treated with NAs, 472 patients without a history of HCC whose FIB-4 was obtained at baseline and after 1 year of treatment were evaluated for the incidence of HCC.
Results: The median age was 54 years and 303 (64.2%) were male. Of 417 patients whose HBV genotypes were determined, 36.9% and 61.2% were genotype B and C, respectively. The median FIB-4 was 2.00 at baseline and was significantly reduced to 1.58 at 1 year ($P<0.001$), but the reduction was small at 2 years or later. The incidence of HCC was significantly higher in patients with FIB-4≥1.58 at 1 year than in those with FIB-4<1.58 (14.8% vs. 3.6% at 10 years, $P<0.001$). When a FAL-1 score, defined as the applicable number of FIB-4≥1.58 and ALT≥31, was scored as 0, 1 and 2, the risk of HCC was significantly higher in patients with a score of 2 than in those with a score of 1 or 0 (24.1% vs. 9.8% vs. 0.7% at 10 years, $P<0.001$).
Conclusion: This study showed that chronic hepatitis B patients with FIB-4 index≥1.58 and ALT≥31 at year 1 of NA had a high risk of HCC.

Workshop 9 [Hepatitis C, Hepatitis B]
WS9-2 10108

MxB Induced in Mitochondria by IFN Inhibits HBV Replication by Activating the RIG-I Signaling Pathway

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Background/Aim: The role of IFN-induced myxovirus resistance protein 2 (MxB) in HBV infection remains unclear. Recently, it was reported that MxB localizes to the inner membrane of mitochondria. Our objective was to determine whether MxB is involved in the innate immune response to HBV via the mitochondrial pathway.
Methods: HBV-expressing and HBV-infected cells were used to evaluate the downstream signaling pathway of RIG-I after knockdown or overexpression of MxB. Liver samples from HBV-infected patients were used to evaluate MxB expression.
Results: Knockdown of MxB significantly increased HBsAg and HBV-expressing cell envelope proteins in culture supernatants. Therefore, MxB may suppress HBV replication primarily by downregulating the expression of envelope proteins. When cells were stimulated with poly(I:C) and downstream signaling of RIG-I was observed, knockdown of MxB inhibited phosphorylation of TBK1 and IRF3. MAVS clustering on mitochondria is thought to be required for this pathway, but MAVS clustering was inhibited by MxB knockdown. MxB mRNA levels in liver samples from patients with chronic and acute hepatitis B were lower than those from patients with chronic hepatitis C. MxB mRNA levels correlated with serum albumin and platelet counts, suggesting that liver fibrosis may progress more rapidly in patients with low MxB expression.
Conclusion: MxB may be required for the downstream pathway of RIG-I. Efficient induction of MxB may be an option for controlling HBV infection.

Workshop 9 [Hepatitis C, Hepatitis B]
WS9-3 10031

HCV Clearance Improves Amino Acids Imbalance in Patients with Hepatitis C Regardless of the Presence of Advanced Fibrosis or Previous Treatment of HCC

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Background: HCV infection induces metabolic disorder on glucose, lipid, and amino acids. However, the impact of antiviral treatment on the imbalance of free amino acids (AAs) in HCV patients remains unclear. This study aimed to elucidate the relationship between AAs, hepatic function and fibrosis following DAA therapy.
Methods: We retrospectively enrolled 189 HCV patients (72 with HCC and 117 without HCC) whose biochemical data and 23 AAs were measured before and after DAA treatment during 2006 to 2022 (mean observational period: 50±27 months).
Results: All non-HCC patients achieved SVR. In comparison of AAs before and after the DAA therapy, ratios of BCAA, cystine and tryptophan to total AAs increased, while ratios of tyrosine (Tyr) and phenylalanine (Phe) decreased, thus leading to the improvement of Fischer's ratio (BCAA/Tyr+Phe). Such changes were more evident in cases with advanced fibrosis. The changes of Fischer's ratio were positively correlated with the changes of M2BPGi, FIB-4, and ALBI score. Interestingly, the changes of Tyr and Phe were negatively correlated with those of M2BPGi, FIB-4, and ALBI score, whereas BCAA changes were not. In HCC-treated patients, 24 cases (33%) received DAA therapy and 23 cases achieved SVR. Similar improvements of AAs imbalance were observed in HCC-treated patients. Furthermore, the duration of time after SVR was positively corelated with Fischer's ratio.
Conclusion: Clearance of HCV led to an improvement of AA imbalance, particularly in advanced fibrosis or curatively-treated HCC patients, suggesting the close association of HCV infection with AA metabolism. The impact of the AAs restoration on hepatocarcinogenesis in SVR patients is further warranted.

Workshop 9 [Hepatitis C, Hepatitis B]
WS9-4 10033

Clinical and Imaging Features of Hypervascular De Novo Hepatocellular Carcinoma after HCV Eradication

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Background: Preneoplastic nodules in hepatobiliary phase hypointensity of EOB-MRI is a risk factor for HCC after SVR. However, de novo hepatocarcinogenesis has been observed in some cases, and the pathogenesis of hepatocarcinogenesis after SVR is unclear. We evaluated hypervascular HCC after SVR and investigated factors involved in hepatocarcinogenesis.
Methods: We identified 90 patients underwent follow-up EOB-MRI after SVR, resulting in 39 hypervascular HCC being reviewed. HCC were divided into two groups: the multistep group showed preneoplastic nodules before hypervascularization, the new group did not show. We investigated characteristics of hepatocarcinogenesis after SVR. We identified 212 hypovascular nodules and nodules achieved SVR were divided into two groups: the first group included nodules observed before SVR, the second group included nodules observed after SVR. We investigated whether temporal relationship between the appearance of preneoplastic nodules and SVR is associated with incident HCC.
Results: Of 39 hypervascular HCC after SVR, 56.4% was in the multistep group and 43.6% was in the new group. The median time from SVR to occurrence hypervascular HCC in the new group was 79.4 ±85.2 days and significantly longer than the multistep group (p&It;0.05). Fat-containing lesions were significantly lower in the new group (11.7%) than in the multistep group (45.5%) (p&It;0.05). Cumulative incidence of hypervascularization showed no significant differences in nodules observed before SVR, nodules observed after SVR.
Conclusions: 40% of newly developed hypervascular HCCs after SVR did not have preneoplastic nodules. Even if there were no preneoplastic nodules before SVR, careful surveillance may be required.

Workshop 9 [Hepatitis C, Hepatitis B]
WS9-5　10109

Recurrence and Prognosis of Patients with Primary Hepatocellular Carcinoma Treated with Radiofrequency Ablation

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Background: To evaluate the relationship between background liver disease and the clinical outcomes of HCC, we investigated patients with HCC treated by RFA, and also examined the risk of alcohol consumption.
Method: We investigated the recurrence and prognosis of 335 newly diagnosed HCC patients treated with RFA from January 2014 to December 2022. We examined the following issues: (1) In patients with HCV, comparison between a group that HCC occurred after Sustained Virological Response (SVR) (SVR-HCC) and a group that SVR was obtained after curative RFA (HCC-SVR), (2) Comparison between the SVR group (SVR-HCC + HCC-SVR) and other etiology groups, (3) the impact of alcohol consumption on recurrence and prognosis.
Results: Etiology was 165/42/62/44/22 for HCV/HBV/Alcohol/NASH/others, respectively. Among HCV, 77/51/37 were SVR-HCC/HCC-SVR/untreated, respectively. (1) There was no difference in recurrence or prognosis between the SVR-HCC group and the HCC-SVR group. (2) Compared to the SVR group, the HBV group showed no significant difference in both recurrence and prognosis, but the alcohol and NASH group had significantly higher recurrence rates (p&It;0.05). (3) In the SVR group, recurrence was significantly lower in the never drinking history group (p&It;0.05). In the alcohol group, patients who abstained from alcohol after HCC treatment tended to have a better prognosis than those who continued to drink.
Conclusion: Since there was no difference in clinical outcomes regardless of the timing of SVR, HCV should be eradicated timely. Abstinence from alcohol may prolong the prognosis in alcohol-based HCC patients.

Workshop 10 [Radiotherapy, Imaging & Diagnosis, irAE]
WS10-1 10111

Effectiveness of Repeated Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma

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The present study retrospectively evaluated the efficacy of stereotactic body radiation therapy (SBRT), including repeated SBRT, for hepatocellular carcinoma. Participants comprised 220 HCC patients treated with SBRT between December 2008 and December 2021. Median overall survival (OS) and disease free survival were 52 months and 17 months, respectively. The 5 years local tumor recurrence rate was 3.4% . Fifty three patients underwent repeated SBRT (twice, 53 cases; three times, 10 cases; four times, 4 cases; five times, 1 case). Median interval between first and second SBRT was 20 months. Median OS from first SBRT was 76 months. Among patients with repeated SBRT, only one case showed local recurrence after second SBRT. Albumin-bilirubin score increased significantly from 6 to 12 months after repeated SBRT, both in the same segment and in remote segments, but the increase was not significant in the same segment. Only one case of grade 3 bile duct stricture was observed in patients who were treated with repeated SBRT. In conclusion, repeated SBRT provides good local control and a low risk of side effects.

Workshop 10 [Radiotherapy, Imaging & Diagnosis, irAE]
WS10-2 10120

Establishment of Hepatic Tumor Differentiation and Hepatocellular Carcinoma Grading Method by Quantitative Analysis of Contrast-enhanced Ultrasound Images Using Microbubbles

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Background: Liver tumors are closely related to blood flow. Contrast Vector Imaging (CVI) is a system that tracks, records, and analyzes the trajectory of microbubbles at a high frame rate. We performed contrast-enhanced ultrasonography (CEUS) of liver tumors and intra-tumor blood flow analysis using CVI to investigate its usefulness in qualitative diagnosis of liver tumors and grading of HCC.
Methods: Subjects included 103 nodules in 103 from June 2019 to February 2020. Tumors included 78 HCC, 14 HEM, 6 FNH, and 5 HCA. Aplio i800 (Canon) was used. The ROI was placed over the entire tumor area, and velocity , direction (In-Flow ratio), and density were measured for 3 seconds from the baseline. For the 70 HCCs that underwent dynamic CT, the contrast pattern of CT was classified as Type 1-4, reflecting tumor differentiation.
Results: Velocity by liver tumor was 25.3/20.2/25.7/24.5 mm/s for HCC/HEM/FNH/HCA, showing no difference between groups. On the other hand, In-Flow ratio was 0.59/0.64/0.37/0.53, showing significantly higher HEM and significantly lower FNH. Density was 6.28/6.99/3.56/10.3 cm2, showing significantly higher HCA ($P<0.05$). CT contrast in HCC cases Velocity by pattern was 19.8/21.9/22.5/26.9 mm/s for Type-1/2/3/4, showing an increase in Velocity with a decrease in predicted differentiation ($P<0.05$).
Conclusion: The usefulness of CVI in qualitative diagnosis of liver tumors and grading of hepatocellular carcinoma has been demonstrated; quantitative assessment of fine blood flow in liver tumors using CVI has the potential to improve the objectivity of CEUS.

Workshop 10 [Radiotherapy, Imaging & Diagnosis, irAE]
WS10-3 10062

Differentiation of AST/ALT Elevation during Immunotherapy in Patients with Advanced Hepatocellular Carcinoma and Other Cancers

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Objective: Immune checkpoint inhibitors (ICIs) for hepatocellular carcinoma (HCC) are more likely to induce liver injury than ICIs for other cancers. However, it is unlikely that immune-related adverse events (irAEs) are the sole cause of liver injury in ICI therapy for HCC. We compared the causes of elevated AST/ALT during ICI treatment for HCC and other cancers.
Methods: A total of 165 patients who received atezolizumab/bevacizumab for advanced HCC between October 2020 and September 2021 in the multicenter cohort (cohort1) and 699 patients who received anti-PD-1/PD-L1 antibody (cohort2) or in combination with anti-CTLA-4 antibody (cohort3) for other cancers between October 2014 and September 2021 at our institution were included in the analysis. Data on AST/ALT elevation were collected retrospectively, and the causes and risks of AST/ALT elevation were analyzed.
Results: The incidence of AST/ALT elevation (grade 2 or higher) was 13.3% (22/165) in cohort 1, 8.5% (55/646) in cohort 2, and 20.8% (11/53) in cohort 3. Among patients with grade 2 or higher AST/ALT elevations, irAE was diagnosed in 13.5% (3/22) in cohort 1, 34.5% (19/55) in cohort 2 and 63.6% (7/11) in cohort 3. The cumulative incidence of AST/ALT elevations in cohort1 was higher in the group with intrahepatic tumor volume greater than 50% ($p=0.002$). The cumulative incidence of AST/ALT elevations in cohorts 2 and 3 was higher in the group with liver metastases ($p<0.001$) and concomitant anti-CTLA-4 therapy ($p=0.004$).
Conclusions: Identifying tumor-related causes of AST/ALT elevations is crucial, particularly in the HCC population.

Workshop 10 [Radiotherapy, Imaging & Diagnosis, irAE]
WS10-4 10121

The Current Status of IMH in Our Hospital and Experience with the Use of Tacrolimus in Cases Resistant to PSL and MMF

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Background: Immune-mediated hepatotoxicity (IMH) is a significant adverse event in cancer treatment with ICIs. However, effective strategies for managing cases resistant to PSL have not been established. This study aims to report the incidence of IMH and the usage of ICIs in our hospital and to suggest ways to manage and deal with them.
Methods: We analyzed 453 patients who received ICI treatment at our hospital between November 2021 and October 2022.Among them, 108 patients were diagnosed with IMH, and cases with grade 3 or 4 were extracted.
Results: The distribution of ICI usage was as follows: Nivolumab 33%, Pembrolizumab 33%, Atezolizumab 14%, Nivolumab+Ipilimumab 12%, Durvalumab 6%, and Avelumab 2%. There were 22 cases (5%) with grade 3 or 4. Consistent with previous reports, the highest incidence was with Ipilimumab (17%). While 14 cases improved with PSL, 2 cases experienced relapse during PSL taper after pulsing. The introduction of MMF was also ineffective. Based on pathological findings of cytotoxic T-cell infiltration in tumor tissue biopsies, adding TAC to the PSL+MMF improved IMH perfectly.
Conclusion: We investigated the incidence and management of IMH in patients undergoing ICI treatment at our hospital. TAC may be an effective treatment option for cases refractory to PSL and MMF.

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

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Ablation has been performed mainly for malignant liver tumors. Ablation has developed through competing with surgery. SURF trial showed no superiority of liver resection over rRFA in terms of OS and RFS. SURF trial is RCT conducted in 49 institutions in Japan. We enrolled patients with HCC of 3 or fewer nodules each 3cm or smaller with well-functioning livers over a 6-year period from 2009, who were then followed for at least 5 years. Regarding the results of SURF trial and other comparative studies, the revised Japanese Clinical Practice Guidelines in 2021 treat resection and ablation equally for patients with HCC of three or fewer tumors, all 3cm or smaller in diameter. From September 2022, RFA for lung, renal, bone, and soft tissue tumors is covered by public health insurance. Since ablation is curative, minimally invasive, can easily be repeated for recurrence, and is cost-effective, it is expected to play an increasingly important role in rapidly aging societies. Japan Academy of Tumor Ablation (JATA) was established for the purpose of enhancing cooperation among members along with related institutions. We aim to achieve safe and effective performances of all ablations, including RFA, MWA, and cryoablation in all areas of the body. Japan is the birthplace of ablation such as percutaneous ethanol injection and MWA. We continue to have the responsibility of leading the world in ablation. We hope many will join us to accumulate clinical experiences and research results, train future generations and contribute to the further development of ablation.

Workshop 11 [Surgery & Transplantation]
WS11-1 10022

Withdrawed.

Workshop 11 [Surgery & Transplantation]
WS11-2 10059

Difficulty in Survival Prediction for Hepatocellular Carcinoma and Cholangicarcinoma after Orthotopic Liver Transplantation

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Objective: To investigate the clinical course of liver cancer, including hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA), after orthotopic liver transplantation (OLT).
Methods: Clinical courses of one hundred eight patients diagnosed with HCC (n=103) or CCA (n=5) were investigated especially in the cancer recurrence after OLT. The liver cancer diagnosis was made via radiological findings before OLT and the clinical courses or pathological findings after OLT. The clinical course after OLT was investigated according to the Milan criteria (within 82, over 21), the 5-5-500 rule (within 90, over 13), and the pathological findings. The pathological findings were as follows, no viable cancer cells (n=16; 15%), well differentiated HCC (n=21; 19%), moderately differentiated HCC (n=62; 57%), poorly differentiated HCC (n=4; 3.7%), and CCA (n=5; 4.6%).
Results: The 10-year survival rates after OLT of patients within and over the Milan criteria were 79% and 59%, respectively, while those of patients within and over the 5-5-500 rule were 76% and 69%. The 10-year survival rate according to the histological findings was as follows: no viable cancer cells, 86%; well differentiated HCC, 65%; and moderately differentiated HCC, 73%. Survival rate of patients with CCA was extremely bad, with a one-year survival rate of 40%. Four of the five CCA patients showed cancer recurrence.
Conclusion: The 5-5-500 rule could not discriminate HCC patients with poor survival. Patients with CCA showed poor survival after OLT.

Workshop 11 [Surgery & Transplantation]
WS11-3 10116

Strategy of Living Donor Liver Transplantation for Unresectable Perihilar Cholangiocarcinoma

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Liver transplantation (LT) for biliary malignancies in Japan is delayed compared to Western countries. This is because of liberal indications for resection in Japan as compared to Western countries and higher technical hurdles in living donor (LD) LT as compared to deceased donor LT, particularly for biliary malignancies. Still, some patients are potential candidates for LT even in Japan, that is, 1. the patients with insufficient liver remnant, 2. the patients with extensive locally advanced disease, which makes vascular reconstruction impossible or extremely difficult, 3. the patients with extensive longitudinal extension, which unlikely gets negative margin even with trisectionectomy, and 4. the patients with PSC, which makes it difficult to determine the area of cancer spread. We launched LDLT program for unresectable perihilar (ph) cholamgiocarcinoma (CCA) in 2018. The main inclusion criteria are unresectable phCCA because of one of the 4 reasons and the exclusion criteria was those with distant or lymph node metastasis. We perform both chemotherapy and radiation therapy as neoadjuvant treatment as a rule. We do stage laparotomy for lymph nodes sampling to rule out LN metastasis a few weeks before LDLT. So far eleven patients with unresectable CCA have been considered for LT, and four patients with phCCA and one patient with intrahepatic CCA underwent LDLT until now. Although all recipients are alive, one patient had recurrent bone metastases. In conclusion, LDLT for unresectable phCCA and iCCA is feasible and can be the last bastion for unresectable CCA. Long-term outcomes should be carefully monitored.

Workshop 11 [Surgery & Transplantation]
WS11-4 10149

Strategy for Liver Transplantation with Marginal Donor for HCC Cases

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Background: The usefulness of liver transplantation as a treatment option for hepatocellular carcinoma has been established, and Japanese guidelines for the treatment of liver cancer recommend liver transplantation for patients with Child-Pugh C liver function. On the other hand, since the number of deceased donors has been deficient in Japan for a long time, most liver transplants have been performed as living donor liver transplants (LDLT); liver transplantation has been positioned as an exceptional treatment option that requires the presence of a living donor. However, the number of deceased donors has been steadily increasing.
Methods: We review our experience with liver transplantation and discuss the marginal donor criteria for HCC cases.
Results: In our department, only 7 DDLTs were performed in the 24 years from 1997 to 2021, but 10 DDLTs were conducted from 2022. We believe that liver transplantation practice has entered a completely different phase. In our department's most recent one-year period, we performed DDLT with a marginal donor in a patient with HCC with a waiting period of 54 days with a low MELD score of 13. The patient had no complications, such as rejection, and the liver transplantation was considered curative.
Conclusion: The rate of cancer recurrence after liver transplantation within Japan criteria is very low, and the long-term outcome is excellent. Therefore, starting DDLT registration as early as possible has become essential to avoid missing the opportunity for liver transplantation in cases where remnant liver function is declining.

Workshop 11 [Surgery & Transplantation]
WS11-5　10110

Laparoscopic Left Medial Sectionectomy According to Tumor Localization

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Background: The standardization of laparoscopic left medial sectionectomy according to tumor localization has been required.
Methods: In the standard approach for the tumor inside S4, first, dissection from the caudal to cranial side along the falciform ligament and umbilical portion dividing G4 was performed. This provides the demarcation line, exposure of UFV and loot of MHV. Next, liver parenchymal transection along MHV from cranial to caudal side was performed, and then cutting line on the caudal side of liver parenchyma was dissected. Finally, the cutting line on the right side of tumor can be divided along to the demarcation line. However, there is a difficult case to apply the standard approach such as the tumor close to the hilum due to a limited space between tumor and hilum. In such a case, the hilum last approach after total parenchymal dissection were useful because this approach provides a clear view of the hilum.
Result: A total of 11 patients (HCC, 7 cases; CCC, 2 cases; Meta, 2 cases) underwent laparoscopic left medial sectionectomy from April 2016. The median size of tumor was 3.75 cm. Median difficulty score was 8 points, median operation time was 494 min, blood loss was 169 ml, and postoperative stay was 12 days. No one required conversion to an open procedure. Although there were 2 cases who had Clavien-Dindo grade 3 complications, no postoperative bile leakage was observed.
Conclusion: Laparoscopic left medial sectionectomy can be achieved safely by changing the approach according to tumor localization.

Workshop 12 [Surgery & Transplantation, TACE, HAIC & Vascular Interventions]
WS12-1 10063

The Impact of Local Ablation in Resected Hepatocellular Carcinoma

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Introduction: Hepatocellular carcinoma (HCC) has a high recurrence rate after curative treatment, and additional treatment of recurrent lesions is important to improve prognosis. HCC is often treated with non-surgical resection, including local ablation(LA), at the time of initial diagnosis, but the impact of LA on the subsequent course of treatment is not clear. In this study, we investigated the effect of previous LA on histopathological findings and prognosis in patients undergoing first-time hepatic resection for HCC.
Methods: Among liver resections for HCC performed at our department from October 2003 to July 2021, 194 cases of liver resection for HCC with no previous treatment and 38 cases of liver resection with previous LA treatment were included. Patient background, perioperative factors, histopathological findings, and prognosis were compared.
Results: There was no significant difference in overall survival from initial treatment or survival after hepatic resection between the initial group and the LA group, recurrence free survival(RFS) after liver resection was significantly shorter in the LA group (982 vs 455 days, $p < 0.01$). In multivariate analysis, multiple tumors, serosal invasion, tumor diameter >3 cm, the history of LA were independent risk factors for RFS. In the risk factor analysis for serosal invasion, the history of LA was an independent risk factor for serosal invasion on multivariate analysis but not for venous or portal vein invasion.
Conclusion: Patients with HCC previously treated with LA have a risk of serosal invasion and postoperative recurrence, which may aid in the choice of surgical technique during salvage liver resection.

Workshop 12 [Surgery & Transplantation, TACE, HAIC & Vascular Interventions]
WS12-2 10130

Ferroptosis is Induced by Lenvatinib through Fibroblast Growth Factor Receptor-4 Inhibition and Play a Key Role in the Suppression of Hepatocellular Carcinoma

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Background: Nrf2 plays an important role in the survival and proliferation of cancer cells. Lenvatinib is a therapeutic agent for the treatment of unresectable hepatocellular carcinoma (HCC), but its relationship with ferroptosis and Nrf2 is unknown. We investigated the relationship between Nrf2 and cell death by lenvatinib in HCC.
Methods: Lenvatinib, erastin, a ferroptosis inducer, and ferrostatin-1 (fer1), a ferroptosis inhibitor, were administered to HCC cell lines, and expression of ferroptosis-related proteins, lipid peroxide, and cell viability were measured. Fibroblast growth factor receptor 4 (FGFR4) was knocked down and the expression of ferroptosis-related proteins, lipid peroxide, and cell viability were measured. We generated high and low Nrf2 expression cell lines and examined the effect of lenvatinib. To examine the expression of FGFR4 and the effect of lenvatinib.
Results: Lenvatinib and erastin treatment of HCC cell lines resulted in decreased expression of ferroptosis-related proteins, generation of lipid peroxide, and decreased cell viability. FGFR4 knockdown decreased the expression of ferroptosis-related proteins, generated lipid peroxide, and decreased cell viability. Lipid peroxide production was suppressed and cell viability was reduced in Nrf2-high expressing cells, while lipid peroxide production was enhanced and cell viability was reduced in Nrf2-low expressing cells. The high FGFR4 expression group was more effective with lenvatinib.
Conclusions: Lenvatinib suppresses FGFR4 and induces ferroptosis. Nrf2 suppresses lipid peroxidation by lenvatinib and avoids ferroptosis.

Workshop 12 [Surgery & Transplantation, TACE, HAIC & Vascular Interventions]
WS12-3 10097

Hyperamylasemia after Hepatic Resection

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Aim: Hyperamylasemia often occurs after hepatectomy, but the detailed mechanism of this phenomenon remains unclear. The aim of this study was to analyze factors that may be associated with the development of hyperamylasemia following hepatic resection.
Methods: 23 patients underwent hepatic resection for primary or secondary liver tumors without concomitant resection of gastrointestinal or pancreaticobiliary tract. Pringle maneuver was used for 12 patients (Pringle group), hemihepatic vascular occlusion for 11 patients (Hemihepatic group). Serum amylase and creatinine levels were measured on the preoperative day and on postoperative days 1,2,4,7,10 and 14. There was no significant difference in age,ICGR15 between the Pringle and Hemihepatic group.
Result: 1.Preoperative and Postoperative Serum Amylase Level:In the Pringle group, serum amylase levels were increased significantly on postoperative days 1,2,4,7 and 10 in comparison to the preoperative levels. In contrast, postoperative serum Amylase levels did not increase significantly in the Hemihepatic group.Significant differences were noted in serum Amylase levels between the Pringle group and Hemihepatic group on postoperative days 1,2,4,7,10 and 14. 2.Preoperative and Postoiperative Serum Creatinine levels: All patients had well-compensated liver functions without ascites and they had normal Cr level pre and postoperatively.
Conclusion: It is suggested that portal congestion by portal triad interruption (Pringle maneuver) carries a potential risk of serum Amylase elevation after hepatectomy.

Workshop 12 [Surgery & Transplantation, TACE, HAIC & Vascular Interventions]
WS12-4 10064

The Effectiveness of the Locoregional Treatment Using Hepatic Arterial Infusion Chemotherapy New FP for Locally Progressed Hepatocellular Carcinoma

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Background: Hepatic arterial infusion chemotherapy (HAIC) has been developed as the treatment for advanced HCC. On the other hand, many systemic therapies are approved now. In the study, we compared the effects of HAIC and sorafenib (Sora) for various tumor conditions.
Methods: We retrospectively corrected the data of 1,709 patients with HCC. The HAIC regimen was New FP, a fine-powder CDDP suspended with lipiodol and 5-fluorouracil. Among them, we included 1,262 patients with Child-Pugh class A (New FP: 418, sora: 844) Then, we evaluated the prognosis of patients in four subgroups after propensity score matching; cohort1 [without (w/o) macrovascular invasion (MVI) and extrahepatic spread (EHS)], cohort2 [with MVI and w/o EHS], cohort3 [w/o MVI and with EHS] and cohort4 [with MVI and EHS].
Results: In cohort1, each median survival time (MST) of the New FP and Sora groups is 20 and 17 months, (n.s.). In cohort2, the MSTs are 19 and 8 months ($p<0.0001$). In cohort 3, the MSTs are 13 and 7.5 months (n.s.). In cohort4, the MSTs are 8.8 and 4 months ($p<0.001$) The presence of major portal vein tumor thrombus, and EHS were independent poor prognostic factors, and Child-Pugh score of 5, the better therapeutic response, and choosing New FP were independent better prognostic factors.
Conclusion: A Powerful locoregional treatment HAIC, in particular, New FP was effective for HCC with MVI regardless of the presence of EHS. In the era of systemic therapies in HCC, HAIC should play an important role to prolong the survival of patients with advanced HCC.

Effect of Distal Splenorenal Shunt plus Splenopancreatic Disconnection on Glucose and Amino Acid Metabolism

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Aims: The Warren-Zeppa distal selective splenorenal shunt (DSRS) is aimed at decompressing esophageal varices by a distal splenorenal shunt, at the same time ligaturing left gastric, gastroepiploic and umbilical veins. In the long-term follow up the loss of shunt selectivity was observed in several cases. Therefore, Inokuchi and Warren reported splenopancreatic disconnection (SPD) to prevent splenic collaterals from stealing portal venous blood.
Methodology: This report presents metabolic data (K-glucose, Insulin (IRI) in iv-GTT(20g/2min),Fischer ratio) of 10 cirrhotic patients operated with DSRS plus SPD.iv-GTT: Venous blood samples were taken from an antecubital vein prior to 20g glucose/2min administration and at 3,5,10,20,30 and 60 min thereafter. Blood glucose, insulin (IRI) and the glucose disappearance rate(K-glucose) were measured.
Results: 1.iv-GTT: 1. K-glucose value was 2.3±0.2 in the pre-shunt group,2.5±0.2 in the post-shunt group.2.IRI dynamics: After loading, serum levels reached their peak in 3 min in both groups with peak values .At 3 min after loading, the pre-shunt group showed significantly higher value than the post-shunt group. Thereafter from 5 min to 10 min, serum IRI decreased gradually. But from 20 min to 60 min, serum IRI increased gradually in both groups. There was no difference in both groups from 5 min to 60 min. 3. Fischer ratio was also improved from 1.58±0.2 to 2.0±0.2 after the operation.
Conclusion: From these results it seems that DSRD+SPD has favorable effects on glucose and amino acid metabolism.

Workshop 13 [Tumor Markers & Biochemistry, CCC, Others]
WS13-1 10051

Diagnostic Value of Serum GPC3 in Early Stage of HCC

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Hepatocellular carcinoma (HCC) is a common cause of cancer related death in Mongolia. Early diagnosis is the very important management to increase successful treatment and survival rate. Glypican-3 (GPC3) protein is highly expressed in hepatocellular carcinoma (HCC) tissue and in serum of HCC patients. Recent studies have been conducted and suggested as a diagnostic biomarker for detecting HCC in the early stage. Therefore, we investigated the diagnostic value of the serum GPC3 level and compared it to the alpha-fetoprotein (AFP) level as a diagnostic biomarker of HCC. We enrolled a total of 90 participants and divided into 3 groups with HCC (30), with liver cirrhosis (LC/30) and healthy (30) as the control group. GPC3 and AFP serum (sGPC-3, sAFP) levels were measured using commercially available enzyme-linked immunosorbent assay kits. The diagnostic accuracy was analyzed using the receiver operating characteristics (ROC) curve and estimated sensitivity and specificity of each biomarker. sGPC3 was significantly elevated in the HCC group as compared to LC and healthy subjects (658±138.2 pg/ml, 378±25.5 pg/ml, 356.3±29 pg/ml) respectively. sGPC-3 sensitivity was 96.6% and specificity was 100%. The area under the ROC curve (AUC) for GPC3 was 0.999 (0.996-1.0). In comparison, the mean of AFP was significantly higher in HCC (16.9±11.7 ng/ml) than in LC (6.7±7.6 ng/ml) and in healthy subject (3.3±2.1 ng/ml) and AFP sensitivity was 43,3 % , specificity was 95 % with an AUC of 0.808 (0.696- 0.921). sGPC3 has a higher sensitivity than AFP for the early diagnosis of HCC.

Workshop 13 [Tumor Markers & Biochemistry, CCC, Others]
WS13-2 10086

Metabolic Profiling Identifies Key Metabolic Biochemical Pathways Associated with Recurrence of Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths worldwide. The metabolic biochemical pathway disturbances associated with HCC progression and recurrence remain unsatisfactorily characterized. Dysregulated metabolism is a hallmark of cancer including HCC, manifested through alterations in metabolites. The emerging field of metabolomics has increased the hope of discovering metabolites and biochemical pathways as the novel biomarkers or therapeutic targets of HCC and tracking tumor recurrence. Here, we performed comprehensive global metabolomics profiling on twenty matched HCC tumor/normal tissue pairs and found that HCC recurrence is characterized by increasing glycolysis and glutaminolysis. Random Forest classification comparing tumor vs. adjacent margin tissues and recurrent vs. non-recurrent tumors using named metabolites gave a predictive accuracy of 96% and 70%. Tumor recurrence was significantly associated with increasing of glucose, pyruvate, alpha-ketoglutarate and NAD+/NADH metabolites to increase glycolysis and glutaminolysis. Higher acylcarnitine levels in non-recurrent HCC indicate elevated fatty acid beta-oxidation. Besides, we also found that Coenzyme A levels were higher and plasmalogen lipids were uniformly lower in recurrent HCC. In conclusion, our study generates a comprehensive metabolomics dataset on HCC and highlight the massive reorganization of cellular metabolism as tumors progress and acquire recurrence feature.

Workshop 13 [Tumor Markers & Biochemistry, CCC, Others]
WS13-3 10112

The Bile Level of Cytokeratin 7 as a Diagnostic Marker for Cholangiocarcinoma

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Background and Aim: Cholangiocarcinoma is a heterogenous and aggressive biliary tract tumor, whose prognosis is very poor. Challenging accurate diagnosis and late presentation with difficult–to–treat stage and obstructive jaundice urge the need for vital discovery of diagnostic alternatives. Our aim is to assess the potential role of cytokeratin 7 in bile as a diagnostic biomarker for cholangiocarcinoma.
Method: A case–control study of 100 subjects, cholangiocarcinoma (n=30), malignant biliary obstruction rather than cholangiocarcinoma (n=20), benign biliary obstruction (n=20), and control (n=30). Bile samples were collected during endoscopic retrograde cholangiopancreatography (ERCP) or cholecystectomy for control group. cytokeratin 7 level in bile samples was analyzed using Enzyme–linked Immunosorbent Assay.
Results : Mean age 57 (±13) years, 60% male. All cholangiocarcinoma is perihilar, other malignancies were (12 cancer pancreas & 8 hepatocellular carcinoma). Cytokeratin 7 in bile was markedly elevated in cholangiocarcinoma (mean 1555.4±302.7 pg/ml) compared to other malignancies(581.9±227.5 pg /ml), benign obstruction (439.5±255.7 pg/ml) and in control group (53±26.4 pg/ml) ($p < 0.001$). A bile cytokeratin 7 cut–point of >1030 pg /ml yielded area under curve (AUC) of 1 (95% CI: 1.000–1.000), 100% sensitivity, 100% specificity, while CA19–9 cutoff >1057 U/mL presented (AUC 0.98) (95% CI: 0.961–1.000), 93.3% sensitivity, 95% specificity ($p < 0.001$). When cholangiocarcinoma stratified by association with cholangitis (17/30), performance of cytokeratin7 remains excellent: AUC of 0.905 (95% CI: 0.847–0.964) in non–cholangitis associated cholangiocarcinoma($p < 0.001$), while Ca19–9 had a two-fold increase in response to infection ($p < 0.05$).
Conclusion: The bile level of Cytokeratin 7 demonstrates outstanding performance that could help the diagnosis of cholangiocarcinoma.

Workshop 13 [Tumor Markers & Biochemistry, CCC, Others]
WS13-4 10023

Withdrawed.

Workshop 13 [Tumor Markers & Biochemistry, CCC, Others]
WS13-5 10141

Efficacy of NewFP Therapy for Unresectable Advanced Intrahepatic Cholangiocarcinoma

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Background: Chemotherapy for unresectable Intrahepatic Cholangiocarcinoma (ICC) is under discussion. We evaluated the efficacy of NewFP(NFP) compared with gemcitabine + cisplatine(GC) therapy for unresectable ICC.
Methods: Patients with unresectable ICC who underwent chemotherapy between March 2017 and March 2023 were recruted in this study. NFP consisted of 50 mg CDDP on Days 1 and 8 followed by 1500 mg 5-FU every 2 months. The dose of GC was 2 doses and 1 rest as 1 course. The therapeutic effect was evaluated by CT.
Results: There were 15 patients in the NFP group and 15 in the GC group. Median age is 70(48-81)/67(47-83), male(12/6) and female(3/9), stage is IVa/IVb/postoperative-recurrence (7/7/1, 2/13/0) respectively. The NFP group was performed GCS/GC/GS/TS1/untreated(1/2/1/1/10) before NFP, and the GC group was the first treatment in all cases. The mean treatment courses in the NFP and GC groups were 6(3-23) and 5.7 (1 -14). With regard to antitumor effects, in the NFP group, PR(7), SD(6), and PD(2), and the DCR was 86.7%. In the GC group, PR(2), SD(6), and PD(7), and the DCR was 53.3%, with more PR in the NFP group. Median tumor shrinkage (NFP/GC) was 18.2%/11.4%, time to best response was 114/82days, and median observation period was 185/151days.
Conclusion: NewFP is a relatively safe and effective local treatment for unresectableICC. In the future, it is necessary to further increase the number of cases and investigate the combination with systemic chemotherapy.

Workshop 13 [Tumor Markers & Biochemistry, CCC, Others]
WS13-6 10136

Support and Implementation System for Clinical Cancer Research at Designed Hospital for Cancer Genomic Medicine and the Prefectural Designated Regional Cancer Hospital

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Background: Yamanashi prefectural central hospital (YCH) was designated as prefectural regional cancer centers and hospital in 2006. In March 2023, YCH was designated as hospital for cancer genomic medicine, plays a central role in Yamanashi prefecture.
Methods: In 2013, YCH established Ambulatory Therapeutic Cancer Center and Genome Analysis Center (GAC). Genome ethics committee was set up and informed consent and a genetic counselling system established in accordance with the joint guidelines of the three ministries. Clinical and genomic information is managed by two full-time staff. Collection and storage system of frozen specimens was established, and liquid specimens such as blood can be ordered on the electronic medical record. Samples are anonymised and storaged immediately by GAC. Blood sampling for research is available on outpatient with the cooperation of blood collection department. Research progress is discussed at monthly meeting for presenting at conferences and scientific articles.
Results: Informed consent were obtained for 8,893 patients (including 301 with HCC). 1,007 frozen tissue specimens (including 300 HCC) and 43,294 liquid specimens were obtained. Number of analysed specimens is 14,703 up to FY2022, 103 peer-reviewed articles and 365 presentations at conferences. In HCC, analysis of 350 samples in-house HCC panels (72 SMGs: 59,016 aa) from approximately 200 patients has been completed, and all transcriptome data from approximately 300 samples have been obtained. Some data will be presented at the meetings.
Conclusion: It is important to strengthen the support system for clinical cancer research at the hospital for cancer genomic medicine and prefectural designated regional cancer hospital.

APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Abstracts

Onsite Poster Sessions

Onsite Poster Session 1 [Systemic Chemotherapy & Oncology 1]
P1-1 10069

Characteristic of HCC Patients Achieving Clinical Complete Response Treated with Atezolizumab plus Bevacizumab

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Background: Atezolizumab plus bevacizumab therapy (Atezo/Bev) for the patients with unresectable hepatocellular carcinoma (uHCC) has a highly response rate and may led to complete response (CR) in some patients. However, the characteristics of patients who achieve CR are not clear. In this study, we analyzed patients with uHCC who received Atezo/Bev and achieved clinical CR.
Methods: 79 patients were enrolled among patients received Atezo/Bev, excluding those who were not evaluated by imaging, performed conversion therapy after downstaging. We focused on clinical CR was obtained by Atezo/Bev alone. Clinical CR was defined as CR by mRECIST and remained negative tumor markers (AFP, AFP-L3, and DCP) for at least three months.
Results: Best response were 3/22/37/17 in CR/PR/SD/PD, respectively. Of which, 7 patients achieved clinical CR. All patients were male and median age was 74 years. Child-Pugh class A was noted in 6, while BCLC stage A/B/C was 1/1/5. One patient showed recurrence after discontinuation of Atezo/Bev. The other 6 patients keep still on clinical CR. Interestingly, 2 patients achieved clinical CR after discontinuation of Atezo/Bev due to AEs. One was an impulsive case whose primary and metastatic tumors were disappeared after radiotherapy for bone metastasis. Clinical CR was achieved during or after discontinuation of Atezo/Bev, however, the characteristics were not clear from the clinical course. Immune hot tumor may have clinical CR in tumor microenvironment. We have to conduct tumor microenvironment, and need to induce tumor immunity.
Conclusion: We reported the case series of clinical CR achieved with Atezo/Bev for uHCC.

Onsite Poster Session 1 [Systemic Chemotherapy & Oncology 1]
P1-2 10057

Usefulness of IL-6 as a Therapeutic Response Predictor in Atezolizumab + Bevacizumab Combination Therapy for Hepatocellular Carcinoma

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Background: IL-6 is a cytokine that indirectly exerts anti-tumor immunity.
Purpose: The purpose of this study was to clarify the usefulness of serum IL-6 level as a biomarker in combination therapy with atezolizumab + bevacizumab(AteBev) for hepatocellular carcinoma(HCC).Methods: of 70 patients treated with AteBev for hepatocellular carcinoma, 38 patients whose serum IL-6 levels could be measured. Dynamic computed tomography was performed after 6 weeks of treatment. Blood samples were collected at baseline and after 3 weeks of treatment.
Results: 29 patients were classified as Child A and 9 as Child B. 22 patients had stage III, 12 patients had stage IVA, and 4 patients had stage IVB. (1) Relationship between best effect judgment and IL-6: IL-6 level did not show significant change in the SD+PD group, but a significant increase was observed in the CR+PR group before and after treatment (p=0.017). (2) Comparison of discriminative ability between IL-6 and tumor markers: Comparing the discriminative ability of responders using the pre-treatment and post-treatment changes of AFP, AFP-L3, PIVKA-2, and IL-6, IL-6 was the only significant variable (p=0.046). (3) Relationship between changes in IL-6 and persistence and survival of AteBev combination therapy: In a comparison of 26 patients with elevated IL-6 levels and 12 patients without increased those, Patients with elevated IL-6 had a significantly higher continuation rate of AteBev combination therapy (p&It;0.01) and improved survival.
Conclusion: Changes in serum IL-6 levels in AteBev combination therapy for HCC may allow prediction of treatment efficacy and prognostic stratification at 3 weeks post-treatment.

Onsite Poster Session 1 [Systemic Chemotherapy & Oncology 1]
P1-3 10076

Atezolizumab + Bevacizumab Post-Treatment Strategies and Outcomes

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Purpose: To investigate the selection and outcome of "post-treatment" of ATZ+BEV in real-life clinical practice.
Methods: A retrospective multicenter study was conducted on 53 patients with advanced hepatocellular carcinoma treated with ATZ + BEV from September 2020 to December 2022. The final follow-up date was March 15, 2023. The primary endpoint was the rate of conversion to active post-treatment after PD. Secondary endpoints were PS at the end of ATZ+BEV, liver function, proteinuria, posttreatment therapy, OS after starting posttreatment, OS after starting ATZ+BEV, and OS from the initial diagnosis day of HCC.
Results: The median age was 74 years. 13 patients were Stage III, 12 patients IV-A, 26 patients IV-B, 46 patients Child-Pugh A, and 7 patients B. After ATZ+BEV treatment, 40/53 patients (75%) completed. PS2 or higher at the end of ATZ+BEV was 7/40, Child-Pugh A 27/B 11, proteinuria 3+ 7/40. Post-treatment therapy included lenvatinib in 10 patients, ramucirumab in 2, cabozantinib in 4, TACE in 7, sorafenib in 2, and BSC in 16.The conversion rate to active post-treatment was 41%. MST after initiation of active post-treatment was 9.2 months, MST after initiation of ATZ+BEV was 16.8 months, and MST from the first treatment was 7.0 years.
Conclusion: After completion of ATZ+BEV, post-treatment was possible for patients with preserved residual liver function and PS. The conversion rate to active post-treatment was 41%, and the MST was 9.2 months. It was suggested that post-treatment may contribute to further prolongation of survival.

Onsite Poster Session 1 [Systemic Chemotherapy & Oncology 1]
P1-4 10027

Treatment outcomes of ABC Conversion Therapy at Our Hospital

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Aim: In this study, we examined the treatment outcomes of ABC conversion therapy at our hospital.
Methods: The subjects were 7 cases out of 31 cases in which Atezo/Bev was introduced at our hospital and ABC conversion therapy was performed. We investigated the timing of ABC conversion therapy, its therapeutic effects, and complications in these cases.
Results: The timing of ABC conversion therapy included 6 cases (Group A) in which tumor reduction was not achieved or initial tumor reduction was followed by progressive disease (PD) and 1 case (Group B) in which ABC conversion therapy was performed during drug discontinuation due to side effects. TACE was performed as curative treatment in 6 cases, and hepatic arterial infusion therapy was performed in 1 case. The treatment effects were as follows: CR in 1 case, PR in 4 cases, SD in 1 case, and PD in 1 case. In the CR case, the tumor became PR due to Atezo/Bev, and new lesions appeared in the liver with lymph node metastasis during Atezo/Bev treatment. Therefore, TACE was performed for the liver lesions, and Atezo/Bev was resumed, resulting in the disappearance of lymph node metastasis and complete response.
Discussion: In ABC conversion therapy, it is believed that tumor antigens are released through curative treatment, leading to the activation of the cancer immunity cycle. This is expected to result in a highly effective treatment.

Clinical features of proteinuria During Atezolizumab plus Bevacizumab Treatment

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Background/Aim: Bevacizumab (Bev) therapy for unresectable hepatocellular carcinoma (uHCC) is frequently associated with proteinuria, leading to Bev withdrawal or suspension. However, the current practice of both qualitative urine test and daily protein determination by 24-hour urine storage is burdensome. The aim of this study was to evaluate the frequency and characteristics of proteinuria in atezolizumab plus bevacizumab (Atez/Bev) therapy for uHCC.
Methods: We conducted a retrospective study on 38 patients with uHCC treated with Atez/Bev from 2020 to 2023. Urinary protein was assessed qualitatively using spot urine and urine protein/urine creatinine (Cr) ratio (UPCR) just before treatment. UPCR positivity was defined as UPCR 2 g/g Cr, which is the criteria for Bev withdrawal.
Results: Among the 38 patients (median age 71 years, 32 males, 25 first-line treatment), 22 (57.9%) had proteinuria after initiating Atez/Bev, and 3 (7.9%) had G3 or higher. There were no significant differences in baseline characteristics between the UPCR negative and positive groups. UPCR positivity increased progressively from 0% in the -, ± groups to 48.5% in the 3+ group. About 25% of the 2+ cases had a UPCR of 2 g or higher by qualitative test alone, while about half of the 3+ cases had a UPCR of less than 2 g.
Conclusion: Proteinuria is a frequent adverse event in Atez/Bev therapy for uHCC, with increasing UPCR positivity in higher qualitative grades. The use of a simple UPCR may reduce the burden on both patients and providers and lead to appropriate medication.

Onsite Poster Session 2 [Systemic Chemotherapy & Oncology 2]
P2-1 10030

Therapeutic Efficacy of Conversion Therapy after Systemic Chemotherapy for Patients with Unresectable Hepatocellular Carcinoma

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Aim: Conversion therapy aims to achieve tumor-free and drug-free status for patients with unresectable hepatocellular carcinoma (u-HCC) who have undergone downstaging with systemic chemotherapy. This study investigates the efficacy of conversion therapy in those patients.
Methods: We conducted a single center, retrospective, cohort study. A total of 17 patients with u-HCC who received systemic chemotherapy for at least 3 months and obtained tumor response between April 2018 and May 2023 (complete response; CR or partial response; PR) were included. Patient demographics, overall survival (OS) and progression-free survival (PFS) rates, as well as additional characteristics were investigated.
Results: The subjects consisted of 13 males (76.4%) and the median age was 76 years (59-88). Nine patients were treated with lenvatinib (LEN), and eight patients atezolizumab (ATZ) plus bevacizumab (BV) as primary systemic chemotherapy agents. Among all 17 patients, 3 (17.6%) underwent conversion therapy, including two patients who underwent hepatectomy and one who received ablation. The mean period from systemic chemotherapy to conversion therapy was 15.6 months (8-22). Among 14 patients in the non-conversion group, tumor recurrence occurred in 7 (50%) and 7 (50%) were deceased, respectively. There was no significant difference in OS and PFS rates between the conversion and non-conversion groups. However, three patients who underwent conversion therapy were maintained the drug-free and tumor-free status.
Conclusion: Conversion therapy may improve prognosis for patients with u-HCC who were obtained the downstaging status by systemic chemotherapy. Therefore, it is desirable for u-HCC patients to achieve conversion therapy with appropriate systemic chemotherapeutic agents.

Onsite Poster Session 2 [Systemic Chemotherapy & Oncology 2]
P2-2 10053

The Impact of Bevacizumab Withdrawal on Prognosis in Atezolizumab + Bevacizumab Combination Therapy for Unresectable Hepatocellular Carcinoma

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Background: Atezolizumab + Bevacizumab (Atezo + Bev) combination therapy for unresectable hepatocellular carcinoma (u-HCC) has been shown to be highly effective as first-line therapy. On the other hand, Bev often needs to be withdrawn or discontinued for reasons such as proteinuria or bleeding event. In this study, we examined the changes in efficacy associated with the withdrawal of Bev.
Methods: We compared the efficacy of Atezo + Bev in 76 patients with u-HCC treated with Atezo + Bev for 6 months or longer at our hospital, and compared the efficacy of Bev withdrawal (n=40) and no withdrawal (n=36) during the course of treatment.
Results: Median age was 71 years, 64 males, 12 females, PS 0/1: 72/4, HBV/HCV/NBNC: 11/22/43, Child-Pugh grade: A/B 69/7, mALBI grade 1/2a/2b: 30/23/23, BCLC stage A/B/C: 4/34/38 cases, first-line treatment and second-line or later were 51 and 25 cases, respectively.OS in the Bev withdrawal and no withdrawal groups were not reached and 22.1 months, respectively (p= 0.684), PFS was 12.2 and 11.7 months (p=0.369), and ORR by mRECIST was 70.0% and 66.7% (p=0.755).There was no prognostic stratification shown by the proportion of medication cycles of Bev to Atezo or by the timing of Bev's initial withdrawal.
Conclusions: In the Atezo + Bev combination for u-HCC, there was no difference in prognosis by the presence or absence of Bev withdrawal, and no stratification was demonstrated in the proportion of Bev withdrawal times or in the timing of initial withdrawal.

Onsite Poster Session 2 [Systemic Chemotherapy & Oncology 2]
P2-3 10107

Clinical Factors Associated with the Therapeutic Efficacy of Atezolizumab Plus Bevacizumab in Patients with Unresectable Hepatocellular Carcinoma: A Multicenter Prospective Observational Study

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Background: This study aimed to assess the therapeutic efficacy of atezolizumab plus bevacizumab for unresectable hepatocellular carcinoma (uHCC) and investigate the clinical factors associated with progression-free survival (PFS) and overall survival (OS) in real-world practice.
Methods: Patients with uHCC receiving atezolizumab plus bevacizumab therapy in 19 hospitals were registered before the treatment and observed prospectively.
Results: Of the 222 study patients with the median age of 73 years, 66.2% were treated as their first systemic therapy, and 47.7% and 16.7% had more than four intrahepatic tumors and macrovascular invasion, respectively. The hepatic etiologies were as follows: viral, 54.1%; non-viral, 45.9%. The objective response rate and disease control rate were 22.0% and 70.6%, respectively. The median PFS and OS were 5.7 months and not reached, respectively. Independent risk factors for the shortened PFS were younger age (< 75) (3.9 months vs. 8.6 months), a higher number of intrahepatic tumors (> 4) (4.0 months vs. 7.9 months), macrovascular invasion (2.3 months vs. 6.7 months), and higher NLR (> 3.03) (3.0 months vs. 7.8 months). Non-viral etiology of hepatitis and the presence of prior systemic therapy were not risk factors. Independent risk factors for the shortened OS were a higher number of intrahepatic tumors, macrovascular invasion, higher α-fetoprotein level (> 400), worse Child-Pugh score (> 5), and higher NLR.
Conclusion: Patients with younger age, a higher number of intrahepatic tumors, macrovascular invasion, and higher NLR were expected to have the shortened PFS in atezolizumab plus bevacizumab therapy for uHCC.

Onsite Poster Session 2 [Systemic Chemotherapy & Oncology 2]
P2-4 10098

Proangiogenic Cytokines are Useful Prognostic Markers for the Advanced Hepatocellular Carcinoma Patients with Atezolizumab Plus Bevacizumab Treatment

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Background: Proangiogenic cytokines play important roles in tumor growth. The aim of this study is to examine the usefulness of cytokines as the prognostic biomarker in patients with advanced HCC treated with Atezolizumab plus Bevacizumab treatment.
Methods: We enrolled 62 advanced HCC patients who were treated with Atezolizumab plus Bevacizumab in a prospective cohort study. Serum samples were collected before starting the regimen. We measured serum Angiopoietin-2 (Ang-2), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), Follistatin (FST) and evaluated the prognostic value of these cytokines on progression free survival (PFS) and overall survival (OS).
Results: PFS was short with large tumor number (>4), high &alpha-fetoprotein (AFP), and high FST. Multivariate analysis with these factors revealed that high FST (HR1.99, P=0.037) was the independent risk factor for PFS.OS was short with high Child-Pugh score (>5), large tumor number (>4), high AFP, and high HGF. Multivariate analysis with these factors revealed that Child-Pugh score (>5) (HR3.84, P=0.0034), large tumor number (>4) (HR3.04, p=0.0012), and high HGF (HR8.69, P=0.010) were the independent risk factors for OS.
Conclusions: Proangiogenic cytokines might be key markers for predicting the prognosis of HCC patients with Atezolizumab plus Bevacizumab treatment.

Role of Prognostic Nutritional Index in Predicting Survival during Atezolizumab Plus Bevacizumab Treatment in Unresectable Hepatocellular Carcinoma: A Multicenter Study in Tohoku, Japan

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Background: Nutrition status is a prognostic factor in patients with hepatocellular carcinoma (HCC). We investigated the impact of prognostic nutritional index (PNI) on HCC patients treated with atezolizumab plus bevacizumab (ATZ/BEV).
Methods: We retrospectively analyzed 242 patients with advanced HCC who were treated with ATZ/BEV. PNI was calculated as 10 × (serum albumin level) + 0.005 × (total lymphocyte count). The area under the receiver operating characteristic curve of PNI for predicting prognosis was 0.575 (optimal cut-off value: 43.2). After propensity score matching, the patients were divided into two groups (low and normal PNI, both N=105) based on PNI of 43.2, and we compared the prognosis and clinical characteristics between the two groups.
Results: Patients with low PNI was older (P = 0.018), had worse Child-Pugh score and ALBI score (both P < 0.001), and had higher AFP (P = 0.02) and PIVKA-II (P = 0.015) than those with normal PNI. Significantly fewer patients with low PNI received other treatments after discontinuation of ATZ/BEV than those with normal PNI. All overall survival (OS, median 15.6 vs. 22.4 months, P=0.01), progression free survival (PFS, 3.8 vs. 6.9 months, P=0.033) and post progression survival (PPS, 7.4 vs. 11.6 months, P=0.021) were significantly worse in patients with low PNI than those with normal PNI. Multivariate analysis revealed a significant association of low PNI with OS (hazard ratio 1.858, P=0.024).
Conclusion: PNI is an independent prognostic factor for OS, PFS and PPS in HCC patients treated with ATZ/BEV.

Onsite Poster Session 3 [Systemic Chemotherapy & Oncology 3]
P3-1 10148

Immune-related Adverse Event Occurrence and Treatment Response to Immune Checkpoint Inhibitors in Patients with Gastrointestinal Cancer; Using All Organ Cancers as the Denominator

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Background: Immune related adverse events (irAEs) occur with immune checkpoint inhibitors (ICIs), but there are few reports on the frequency of irAEs in gastrointestinal cancer patients. We aimed to investigate the relationship between the frequency of irAEs and treatment efficacy in patients with gastrointestinal cancer since the introduction of ICIs at our hospital.
Methods: All patients who received ICI from November 2014 to December 2022 were included in the study, and the cancer type, frequency of irAE, etc. were investigated retrospectively, and survival time (OS) with and without irAE in gastrointestinal cancer patients were compared.
Results: ICI was used in 675 patients, 375 (56%) respiratory cancers, 110 (16%) gastrointestinal cancers, 22 of which were liver cancer and 79 (12%) urological cancers. irAE occurred in a total of 264 patients (39.1%), 48% respiratory, 38% urological, and 24% gastrointestinal cancers. The median OS of patients with gastrointestinal cancer with or without irAE was 20.5 months in the treatment group and 10.7 months in the treatment group without irAE (P=0.027). The median OS for all cancer types was 30.6 and 11.9 months in the treatment-exposed and non exposed groups, respectively.
Discussion: Although the patients with gastrointestinal cancers with irAE showed a prolonged OS, the impact was small compared to the OS prolongation in all cancer types. It is interesting that the frequency of irAE in gastrointestinal cancer patients was lower than that in other cancer types, which may have affected OS. irAE expression may be considered a "biophenotype" associated with prognosis.

Onsite Poster Session 3 [Systemic Chemotherapy & Oncology 3]
P3-2 10080

Serum Aldolase Predicts Dose Reduction or Interruption of Cabozantinib in Patients with Hepatocellular Carcinoma

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Background: This prospective study aimed to examine the surrogate marker of dose reduction or interruption of cabozantinib in patients with unresectable hepatocellular carcinoma (uHCC).
Methods: Serum creatine kinase (CK), aldolase (ALD), and each trough concentration of cabozantinib (Ctrough) weekly for 6 weeks after stating treatment were measured.
Results: Twenty-three patients were enrolled in the study. Some patients were started at a reduced dose (40 or 20 mg) of cabozantinib. The rate of first dose reduction or interruption rate was 96% and 77%, respectively. Proteinuria was observed in 73% in any grade. Other frequent AEs were malaise in 65% in any grade. The increase in serum CK in 35% in any grade. Serum CK and ALD values at 1,2,3,4, and 6weeks were significantly higher baseline values. Additionally, the proportion of patients who exceed standard values in serum ALD was 100%. There were significant positive correlations between serum CK and ALD values at 1,2,3,4, and 6 and each Ctrough of cabozantinib at the same time points ($r=0.581$, $p<0.001$; $r=0.664$, $p<0.001$). Receiving operating characteristics (ROC) curve analysis showed that serum CK $\geq$128.5mg/dl and ALD $\geq$ 9.05 mg/dl accurately predicted the onset of dose reduction or interruption of cabozantinib, with an aera under the ROC of 0.688 and 0.804, respectively.
Conclusion: Measurement of serum ALD could be the judgement index to predict the dose reduction or interruption of cabozantinib.

Onsite Poster Session 3 [Systemic Chemotherapy & Oncology 3]
P3-3 10142

The Safety and Efficacy of Combination Immunotherapy of TACE (Transarterial-chemoembolization) and Autologous Natural killer Cells in Patients with Hepatocellular Carcinoma

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Background: Transarterial chemoembolization (TACE) is a main therapy for intermediate hepatocellular carcinoma (HCC). The current study reports results of a prospective trial investigating safety and efficacy of combination of autologous NK cells and TACE in patients with HCC.
Methods: This study enrolled 5 consecutive patients with HCC of intermediate stage from CHA Bundang Hospital in Korea: 80% males, 80% Child class A. All patients underwent TACE followed by autologous NK cell therapy (2~6x10^9 cells, intravenous infusion once a week, 1 weeks after TACE, upto 3 cycles) since January 2023. Tumor response assessed according to modified RECIST criteria. We also analyzed the progression-free (PFS) and overall survival (OS).
Results: At 6 months following combined immunotherapy, 3 of 5 patients (60%) achieved complete response and 2 patients (40%) achieved partial response, the objective response rate 100%. The 6-month PFS and OS rates were 100%, respectively. During a median treatment period of 6 months, the most frequent adverse events were pyrexia (80%), chill (70%), skin rash (50%) and myalgia (30%): there were no grade 4 treatment-related adverse events. The baseline AFP level was 8.47 (mean) ng/ml and decreased to 4.53 ng/ml at 4 weeks after TACE. In PIVKAII, the baseline PIVKAII level was 43.62 mAU/ml and decreased to 30.70 mAU/ml at 4 weeks after TACE (p=0.004).
Conclusion: Adoptive immunotherapy with autologous NK cells is a safe, feasible treatment that can lower recurrence and improve recurrence-free outcomes after conventional TACE for HCC.

Onsite Poster Session 3 [Systemic Chemotherapy & Oncology 3]
P3-4 10071

Impact of Grip Strength in Patients with Unresectable Hepatocellular Carcinoma Treated with Atezolizumab Plus Bevacizumab

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Background & Aims: This study evaluated the impact of sarcopenia-related factors (muscle strength and skeletal muscle mass) on the survival of unresectable hepatocellular carcinoma (u-HCC) patients treated with atezolizumab bevacizumab (ATZ+BEV).
Methods: This observational study enrolled patients with u-HCC who received ATZ+BEV from October 2020 to June 2023 (n=85). A low muscle mass was defined as skeletal muscle index (SMI) <42 and <38 cm2/m2, and low muscle strength was defined as a grip strength (GS) <28 and <18 kg in men and women, respectively.
Results: A decreased GS and decreased SMI were found in 34 and 28 patients, respectively. The median observation period was 10.5 months, with a treatment response rate of 20.7%, disease control rate of 81.0%. The OS of the normal GS group was significantly higher than that of the decreased GS group (P<0.01), while that of the normal and decreased SMI groups did not differ markedly (P=0.65). There were no significant differences in the PFS between the normal GS and decreased GS groups (P=0.08) or the normal SMI and decreased SMI groups (P=0.97). A multivariate cox proportional hazards model showed that modified albumin-bilirubin-grade (mALBI) 2b (hazard ratio (HR) 2.49), AFP > 100mAU/ml (HR 2.04) and a decreased GS (HR 3.56) were independently associated with an increased risk of poor prognosis.
Conclusions: In addition to the hepatic functional reserve and tumor marker, a decreased GS was a poor prognostic factor in patients with u-HCC treated with ATZ+BEV.

Effect of Atezolizumab Plus Bevacizumab Combination Therapy on Skeletal Muscle Mass and Cardiac Function by Age in Patients with Hepatocellular Carcinoma

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Background: We reported that sorafenib, an anti-VEGF inhibitor, may reduce skeletal muscle mass by suppressing carnitine absorption in patients with liver cancer (Anticancer Res 2020 40:4173-4182). However, the effects of the monoclonal antibody VEGF inhibitor Bevacizumab have not been reported.
Aim: Objective: To clarify the age-dependent effects of atezolizumab + bevacizumab (AteBev) combination therapy on skeletal muscle mass and cardiac function in patients with hepatocellular carcinoma (HCC).
Methods: Fifty-five HCC patients treated with AteBev combination therapy in our department were included. Before treatment and 3 weeks after treatment, blood samples were collected. Abdominal CT examination was performed 6 weeks after treatment, and the therapeutic effect was evaluated using mRECIST, and PMI was calculated from the iliopsoas muscle area. In addition, left ventricular systolic function was evaluated using global longitudinal strain (GLS) in echocardiography.
Results: There were 10 middle-aged patients, 19 early-elderly patients, and 26 late-elderly patients. In the study of skeletal muscle mass, PMI after 6 weeks of treatment showed significant changes in middle-aged and early-elderly patients. A significant decrease was observed in the late-elderly patients, although no cardiac function studies showed no significant changes in %Ejection Fraction and GLS after 3 weeks of treatment in middle-aged patients, but significant decreases in early- and late-elderly patients.
Conclusion: Cardiac function decline was confirmed in the elderly patients after 3 weeks of treatment in AteBev combination therapy . In this case, it was considered important to actively introduce nutrition and exercise therapy to maintain not only skeletal muscle mass but also cardiac function.

Onsite Poster Session 4 [TACE, HAIC, Imaging, Radiation]
P4-1 10088

Indications for Arterial Infusion Chemotherapy from the Atezolizumab + Bevacizumab (ATZ+BEV) GTO Cohort- HAIC is Always the Last Line of Defense-

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Purpose: Now that combined immunotherapy has become the mainstay of treatment for advanced HCC, the question is, “Where does HAIC come in?” The purpose of this study was to examine this question.
Methods: Cases treated with ATZ+BEV enrolled in the GTO were included. 1. Validation of the efficacy and safety.2. Efficacy and safety in patients with portal vein tumor invasion.3. Characteristics of cases with PD.
Results: 1. 47 patients treated with ATZ+BEV from October 2020 to October 2021 were included in the analysis. The efficacy was mRECIST: 9 CR, 11 PR, 19 SD, 8 PD. Overall survival was 82.1% at 6 months, 74.2% at 12 months. Regarding safety, the major AEs were hypertension in 22 patients, proteinuria in 22 patients, and fatigue in 13 patients, and some Grade 3 or higher AEs were observed in 19 patients (40%). 2. Seven of 17 patients (41%) with portal vein involvement were associated with distant metastasis: 3 CR, 2 PR, 11 SD, 1 PD, response rate was 29%, disease control rate was 94%. Overall survival was 70% at 6 months and 60% at 12 months, with no significant difference compared with patients without portal vein involvement (p=0.19). 3. Logistic regression was used to identify predictive factors for PD in 15 (32%) patients with ATZ+BEV. However, PD patients had significantly shorter survival than non-PD patients (6-month survival 93% vs. 65%, p=0.01).
Conclusion: Patients who developed PD after A+B treatment seemed to be a good candidate for intravenous infusion.

Onsite Poster Session 4 [TACE, HAIC, Imaging, Radiation]
P4-2 10075

Long-term Prognosis of Stereotactic Body Radiotherapy Versus Radiofrequency Ablation in Patients with Small Hepatocellular Carcinoma Evaluated by Hepatic Reserve, Single-center Study

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Background: Stereotactic body radiation therapy (SBRT) for small HCC has been reported to be as effective as other locoregional therapies. On the other hand, SBRT for small HCC has been also reported to have better local control than RFA (radiofrequency ablation therapy) , but with a poorer prognosis. SBRT is therefore a controversial treatment for HCC and is not recommended in the BCLC 2022 Update. Therefore, we compared the prognosis of patients who underwent SBRT and RFA for small HCC at our hospital.
Method & Result: From 2013 to 2019, SBRT and RFA were performed 68 and 103 cases, as the treatment for small HCC (<3cm, within 3 nodules, Child-Pugh A and B (7-8) and mALBI 1, 2a, 2b), retrospective study. The median observation period after SBRT and RFA was 3.67 and 5.45 years. The overall 5-years survival rate after SBRT and RFA was 56.6% & 76.0%(p=0.003).The post SBRT and RFA 3-years survival rate of mALBI 2b was significantly worse than that of mALBI 1+2a, respectively (SBRT group: mALBI 1+2a vs 2b=90.9% vs 48.2%(p<0.001), RFA group: mALBI 1+2a vs 2b=90.3% vs76.9%(p<0.001)). And the post-SBRT survival rate of mALBI 2b was inferior than the post-RFA survival of mALBI 2b(p=0.004).
Conclusion: SBRT under the condition of mALBI 2b may have inferior long-term prognosis to RFA. The selection of eligible patients for SBRT is important because the prognosis of SBRT cases with mALBI 2b is significantly worse than that of RFA cases and SBRT cases with mALBI 1 and 2a.

Onsite Poster Session 4 [TACE, HAIC, Imaging, Radiation]
P4-3 10106

Comparison of Diagnostic Accuracy between Fibroscan 630 and MR Elastography for Diagnosing Esophagogastric Varices by Measuring Splenic Stiffness

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Objective: Upper gastrointestinal endoscopy can most reliably assess the presence of esophagogastric varices (EGV) in patients with chronic liver disease (CLD) but is also highly invasive. Therefore, attempts have been made to predict the presence of EGV noninvasively, such as the combination of liver stiffness measurement (LSM) and platelet counts proposed in the Baveno IV Consensus. In this study, we measured splenic stiffness measurement (SSM) using FibroScan 630 (FS-SSM) and magnetic resonance elastography (MRE) (MRE-SSM) to investigate the detection of EGV.
Methods: We retrospectively evaluated 54 patients with CLD who underwent FibroScan 630, MRI (3T), and upper gastrointestinal endoscopy from November 2022 to April 2023, measuring FS-SSM and MRE-SSM, and evaluated their diagnostic ability for EGV using ROC curves. The ROC curve was used to evaluate the diagnostic performance of FS-SSM and MRE-SSM.
Results: The diagnostic performance of FS-SSM for EGV was AUROC: 0.90, cutoff: 36.5 kPa, sensitivity: 84.5%, and specificity: 84.5%. The diagnostic performance of FS-SSM for EGV was AUROC:0.90, cutoff: 36.5 kPa, sensitivity: 84.5%, specificity: 91.1%, which was higher than that of MRE-SSM (AUROC: 0.80, cutoff: 11.5 kPa, sensitivity: 50.0%, specificity: 100%).
Conclusion: Diagnostic performance of EGV by FS-SSM was higher than that by MRE-SSM, but it was measured without splenomegaly. it may be necessary to consider the position of the pad when measuring MRE-SSM.

Onsite Poster Session 4 [TACE, HAIC, Imaging, Radiation]
P4-4 10102

The Diagnostic Ability for Microvascular Invasion Using Contrast Enhanced Ultrasopnography

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Background: Vascular invasion in hepatocellular carcinoma (HCC), especially portal invasion, is the important factors correlated with the prognosis. We reported that Micro Flow Imaging(MFI) and the imaging in Kupffer phase using contrast enhanced ultrasound(CEUS) were useful factor for diagnosing the degree of differentiation in HCC. The aim of this study was to investigate the usefulness of MFI in the diagnosis for portal invasion(Vp1-2).
Methods: 115 HCCs from Jun 2015 to Apr 2021 were included. The image of MFI was classified into three categories(fine/ vascular/ irregular).
Results: In univariate analysis, the irregular pattern and non-simple nodular type(Non-SN type) in HCCs were significantly correlated with Vp1 or 2(irregular; odds ratio(OR) 2.51 95%CI; 1.080-5.85, p=0.033. non-SN type; OR 2.80 95%CI; 1.26-6.22, p=0.011). In multivariate analysis, Non-SN type in HCCs was significantly correlated with Vp1-2(non-SN type; OR 2.45 95%CI; 1.080-5.560, p=0.032). In the univariate analysis using the histological gross classification instead of the gross classification by CEUS, the irregular pattern was significantly correlated with Vp1-2(irregular; OR 2.51 95%CI; 1.080-5.85, p=0.033). Sensitivity(Se)/ Specificity(Sp)/Positive predictive value(PPV)/ Negative predictive value(NPV) in the diagnosing Vp1-2 for HCCs with the irregular pattern were 0.39, 0.80, 0.44, 0.76, respectively. Se/ Sp/ PPV/ NPV in the diagnosis Vp 1-2 for HCCs with non-SN type were 0.61, 0.64, 0.41, 0.80, respectively.
Conclusion: The irregular pattern and the non-SN type were the useful factor in the diagnosing Vp 1-2.

Onsite Poster Session 5 [Basic Science & Pathology 1]
P5-1 10044

Clinicopathological Characteristics and Molecular Analysis of Lymphocyte-rich HCC

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Background: Lymphocyte-rich hepatocellular carcinoma (LR-HCC), a newly proposed subtype of HCC described in the WHO classification 5th edition, is characterized with abundant lymphocyte infiltration in the tumor. We examined the clinicopathological and molecular features of LR-HCC.
Methods: We analyzed 451 surgically-resected HCC cases without previous treatment history at our hospital. Clinicopathological characteristics of the LR-HCC and the other HCC (non-LR-HCC) subtypes were compared. Neoplastic and nonneoplastic hepatocytes from LR-HCC (n=4) were collected with a laser microdissection system, and RNA was extracted, followed by microarray analysis to examine molecules involved in lymphocytic infiltration. The immunohistochemical staining of identified molecules was performed in LR-HCC and non-LR-HCC cases. Immunostaining for CD3, CD20, and CD8 was also performed in LR-HCCs.
Results: There were 28 cases of LR-HCC. No statistically significant differences were found in clinicopathological features, except for gross type, between LR-HCC and non-LR-HCC cases. The 5-year survival rate for LR-HCC was over 90%. Microarray analysis revealed that CCL20 was highly expressed in LR-HCC cases and immunohistochemical study showed that CCL20 expression was significantly higher in LR-HCC ($p<0.01$) than in non-LR-HCC. Expression of CCR6, the only known receptor for CCL20, was confirmed in infiltrating lymphocytes in LR-HCC. There were significantly more CD3+ cells than CD20+ cells ($p<0.0001$) in tumor infiltrating lymphocytes, and most of them were CD8+ T cells.
Conclusion: The clinicopathological characteristics of LR-HCC cases were clarified with resected cases of our hospital. CCL20 expression appears to contribute to rich CD8+ lymphocyte infiltration in LR-HCC.

Onsite Poster Session 5 [Basic Science & Pathology 1]
P5-2 10101

Identification of the Possible Target Genes of Hepatoma-derived Growth Factor in Hepatoma Cells

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Background: We have identified hepatoma-derived growth factor (HDGF), which participates in the progression of hepatocellular carcinoma (HCC). Recently, we determined two HDGF-associated microRNAs (miR-6072 and miR-3137) that were related to the prognosis of HCC patients. We further searched for the target genes of these HDGF-related microRNAs.
Methods: Using the microarray method, we determined the mRNAs that increased (&gt1.5-fold) or decreased (&lt0.67-fold) after the administration of HDGF in two hepatoma-derived cell lines (HepG2 and SK-Hep1). Using an open-access databank, we determined the genes that were predicted to be the target genes of both miR-6072 and miR-3137. Finally, we determined genes that were associated with the prognosis of HCC patients.
Results: A total of 1132 genes were considered as common target genes of the 2 HDGF-related microRNAs. Among the 1132 genes, a microarray system showed that 6 genes were increased (&gt1.5-fold) or decreased (&lt0.67-fold) after HDGF administration. Using a cancer genomics database, two of the six genes were found to be related to the prognosis of HCC. A high expression of alkylglycerone phosphate synthase (AGPS) was significantly associated with a poor survival ($p=0.0025$, 0.0063 and 0.0081 for the 1-, 3- and 5-year survival, respectively). A high expression of the shroom family member 4 (SHROOM4) gene was found to be significantly associated with a better survival ($p=0.003$, 0.0006 and 0.0006 for the 1-, 3- and 5-year survival, respectively).
Conclusion: We determined potential target genes of HDGF-related microRNAs that were associated with the prognosis of HCC.

Onsite Poster Session 5 [Basic Science & Pathology 1]
P5-3 10085

Differential Diagnosis of Intrahepatic Metastasis (IM) and Multicentric Carcinogenesis (MC) - How Close can Clinical Indicators Get to the Genome?

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Purpose: We examined the extent to which conventional methods can be used for accurate differential diagnosis of IM and MC by comprehensive genome profile (CGP).
Methods: Patients with HCC who underwent initial resection and re-resection for recurrence were included in the study. CGP analysis was performed using a panel generated in house by In house by 72 hepatocellular carcinoma related genes. We analyzed whether conventional clinical indices can differentiate IM and MC. 1. time of recurrence, 2. site of recurrence, 3. imaging findings, 4. tumor markers, 5. pathological findings, 6. pathological portal vein invasion, by IM and MC.
Results: There were 18 males and 7 females with a median age of 72 years; CGP analysis revealed 11 IM and 14 MC cases. 1. In comparison of conventional differentials, early recurrence; IM 10/11: MC 9/14. 2. site of recurrence; IM (same area 2, other area 9): MC (same 2, other12). 3. Imaging; IM and MC all classically HCC. 4. pattern of tumor marker elevation; IM (concordant 6, discordant 5): MC (concordant 2, discordant 12). 5. Recurrent pathology; IM (6 moderately differentiated, 5 undifferentiated): IM (4 well-differentiated, 9 moderately differentiated, 1 undifferentiated) Edmondson-Steiner classification; IM (II 5, III 6): MC (II 10, III4). 6. Pathologic portal vein involvement; IM (positive in 3/11 cases): MC (positive in 2/14 cases).
Conclusion: It has been difficult to differentiate IM from MC by conventional clinical indices alone. Diagnosis by CGP is necessary for accurate differentiation.

Onsite Poster Session 5 [Basic Science & Pathology 1]
P5-4 10087

Differential Diagnosis of IM and MC by Comprehensive Genomic Profiling (CGP) Changes Treatment Strategies

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Purpose: We examined whether accurate diagnosis of intrahepatic metastasis (IM) and multicentric carcinogenesis (MC) by CGP would change the treatment strategy.
Methods: Patients with HCC who underwent initial resection and re-resection for recurrence were included in the study. Twenty-five cases in which the diagnosis of IM or MC could be confirmed by CGP using resection specimens were included in the analysis. CGP analysis was performed using a panel generated in house by 72 hepatocellular carcinoma related genes. Overall survival by accurate diagnosis of IM and MC were analyzed.
Results: Regarding prognosis from initial resection, IM 5-year survival rate was 55% and MC was alive in all cases.
Conclusion: Accurate diagnosis of IM and MC by CGP may change treatment strategies, with aggressive curative treatment for MC recurrence, while early systemic therapy may be considered for IM.

Onsite Poster Session 6 [Basic Science & Pathology 2]
P6-1 10081

High-fat Diet Promotes Hepatic Fibrosis and Tumorigenesis in a Rat Cirrhosis Model

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Background: Even after removing the cause of chronic liver disease, patients remain at risk for the complications, including liver cancer. In addition, studies have been conducted on nutritional therapy for liver cirrhosis with branched-chain amino acid preparations; however, there are few reports on the effects of lipid intake on the prognosis of cirrhosis. In this study, we examined the effects of a high-fat diet (HFD) on liver cirrhosis using a rat model.
Methods: seven-week-old male rats were orally administered carbon tetrachloride (CCl4) twice a week for 5 weeks to create liver cirrhosis. The rats were then divided into two groups; control chow diet (CD)- and HFD-fed groups. Both groups were further treated with CCl4 twice a week for 5 weeks and dissected at 17 weeks of age.
Results: In HFD group, hepatic fibrosis and steatosis were noticeable despite the discontinuation of CCl4 administration, and the expressions of fibrosis and steatosis markers in the liver were higher than those in CD group. Elevated hepatic mRNA expressions of inflammatory cytokines and exacerbated insulin resistance were also observed in HFD group. In addition, hepatic precancerous lesions developed in all groups, and the incidence and multiplicity in HFD group were higher compared to CD group.
Conclusions: the findings suggest that HFD exacerbates hepatic fibrosis and increases hepatic tumor development even after the etiology of cirrhosis has been eliminated. Nutritional therapy focusing on lipid intake may improve the prognosis of cirrhosis.

Onsite Poster Session 6 [Basic Science & Pathology 2]
P6-2 10049

Dual Angiotensin II Receptor and Neprilysin Inhibitor Attenuates Liver Fibrosis by Preventing Hepatic Stellate Cell Activation

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Background: The natriuretic peptide (NP) system such as atrial NP (ANP) and C-type NP (CNP), a counter-regulatory hormone regulated by neprilysin, has gained attention as a mediator of liver fibrosis and hepatic stellate cell (HSC) activation as well as angiotensin-II (AT-II). Currently, although the combination of an AT-II and neprilysin inhibitor (sacubitril/valsartan: SAC/VAL) showed clinical efficacy in patients with heart failure, its potential effects on hepatic fibrosis have been unclarified. This study assessed the effects of SAC/VAL in murine liver fibrosis as well as the phenotypes of HSCs.
Methods: The effect of SAC (30 mg/kg/day) and/or VAL (30 mg/kg/day) was assessed in CCl4-induced liver fibrosis in C57BL/6 mice. In vitro study was performed to elucidate the change in proliferation and fibrogenic activity of LX-2 cultured with ANP, CNP, angiotensin-II (AT-II)/VAL.
Result: Treatment with SAC and VAL markedly attenuated CCl4-induced liver fibrosis while reducing α-SMA+-HSC expansion and decreasing hepatic hydroxyproline and mRNA levels of pro-fibrogenic markers. Treatment with SAC increased plasma ANP and CNP levels in CCl4-treated mice, and ANP effectively suppressed cell proliferation and TGF-β-stimulated MMP2 and TIMP2 expression in LX-2 cells by activating guanylate cyclase-A/cGMP/protein kinase G signaling. Meanwhile, CNP did not affect the pro-fibrogenic activity of LX-2 cells. Moreover, VAL directly inhibited AT-II-stimulated cell proliferation and expression of TIMP1 and CTGF through the blockade of the AT-II type 1 receptor/protein kinase C pathway.
Conclusion: SAC/VAL may be a have novel therapeutic treatment for liver fibrosis.

Onsite Poster Session 6 [Basic Science & Pathology 2]
P6-3 10018

A Novel Hepatitis Delta Virus (HDV) in Vitro Carcinogenesis Model

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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.
Method: 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.

Onsite Poster Session 6 [Basic Science & Pathology 2]
P6-4 10065

Impact of TIGAR on Malignant Activity and Resistance to Ferroptosis in Intrahepatic Cholangiocarcinoma

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Background: TP53-induced glycolysis and apoptosis regulator (TIGAR) is important gene coding for a regulatory enzyme of glycolysis and reactive oxygen species (ROS) detoxification, and is associated with worse prognosis in various cancer. Ferroptosis is a new type of programmed cell death triggered by iron-dependent lipid peroxidation. There are no reports about the prognostic impact of TIGAR on intrahepatic cholangiocarcinoma (ICC) and its role in ferroptosis is limited.
Methods: 90 ICC patients undergone hepatic resection were enrolled. Immunohistochemical staining for TIGAR was performed. The regulation of malignant activity by TIGAR, and the association between ferroptosis and TIGAR was investigated in vitro.
Results: 22 patients (24.4%) were divided into TIGAR-positive group by immunohistochemical staining. There were no noticeable differences in background factors between two groups, but TIGAR positivity was one of independent prognostic factors in disease-free survival (hazard ratio (HR), 2.00; 95% confidence interval (CI), 1.04-3.85, p=0.0378) and overall survival (HR, 2.10; 95% CI, 1.03-4.30, p=0.0042) in multivariate analysis. In vitro, TIGAR-knockdown (KD) decreased cell motility (abilities of cell proliferation/ migration/ invasion/ colony forming) and elevated ROS and lipid peroxidation. It indicated that TIGAR-KD induced ferroptosis. TIGAR-KD-induced ferroptosis was suppressed by the use of liproxstatin. TIGAR-KD decreased expression of glutathione peroxidase 4, known as factor suppressing ferroptosis, by increasing the NADP+/NADPH ratio and GSGG/GSH ratio. Combination of TIGAR-KD with cisplatin significantly induced more ferroptosis.
Conclusion: TIGAR is associated with poor outcome of ICC patients and resistance to ferroptosis.

Onsite Poster Session 7 [Basic Science & Pathology 3]
P7-1 10054

Investigation of the Association between Receptor Type Tyrosine Kinase Expression and Genetic Variation Using TCGA HCC Data

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Background: Receptor type tyrosine kinases (RTKs) are major therapeutic targets for cancer, and molecular targeted drugs against RTKs, including VEGFR, have been developed for hepatocellular carcinoma (HCC). However, the relationship between RTK expression and genetic mutations remains unclear. In this study, we examined the relationship between RTK gene expression and gene mutations using data from TCGA (The Cancer Genome Atlas).
Methods: Gene mutation and gene expression data of 364 pretreated hepatocellular carcinoma cases were downloaded from the GDAC Firehose browser (https://gdac.broadinstitute.org) and analyzed with the statistical analysis software R. Four or more mutations in 4731 genes were found. For each of the 34 RTKs, a t-test was used to analyze the difference in expression with and without the 4731 mutations.
Results: CTNNB1 mutations had the lowest p-value (p&It;10-4) among 4731 mutations in 13 RTKs expressions. Among them, the expression of FGFR2 was significantly affected by CTNNB1 mutation (p&It;10-38). The TP53 mutation had the lowest p-value (p&It;10-4) in FLT1, KDR, FLT4, TIE1, TEK and RTKs involved in angiogenesis. p-values for HNF1A mutation were lowest in FGFR4 and ROS1, especially in FGFR4, with a particularly strong correlation of p&It;10-24. Discussion: Like the subgroup classification, the effects of CTNNB1 and TP53 mutations were strongly observed in the expression of RTKs. RTKs involved in angiogenesis were also included, suggesting that these mutations may be involved in the cancer microenvironment and affect the efficacy of molecularly targeted drugs.
Conclusion: We investigated the association between RTK expression and genetic mutations in HCC tissues, including the microenvironment.

Onsite Poster Session 7 [Basic Science & Pathology 3]
P7-2 10014

Glucagon-like Peptide-1 Receptor Agonist, Semaglutide Attenuates Chronic Liver Disease-induced Skeletal Muscle Atrophy in Diabetic Mice

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Background: Recent studies have demonstrated the molecular role of the glucagon-like peptide-1 receptor agonist (GLP-1RA) in skeletal muscle homeostasis; however, the therapeutic efficacy of semaglutide, a GLP-1RA, on skeletal muscle atrophy in chronic liver disease (CLD) under the diabetic condition remains unclear.
Methods: We used in vivo diabetic CLD-related sarcopenic models in KK-Ay mice and in vitro atrophy models C2C12 myocytes to investigate therapeutic efficacy of semaglutide.
Result: Semaglutide inhibited psoas muscle atrophy and suppressed declines in grip strength in mice. Moreover, semaglutide inhibited ubiquitin-proteosome-mediated skeletal muscle proteolysis and promoted myogenesis in C2C12 myocytes. Mechanistically, this effect of semaglutide on skeletal muscle atrophy was mediated by multiple functional pathways. First, semaglutide protected against hepatic injury in mice accompanied by increased production of insulin-like growth factor 1 and reduced accumulation of reactive oxygen species (ROS). These effects were associated with decreased proinflammatory cytokines and ROS accumulation, leading to suppression of ubiquitin-proteosome degradation in the skeletal muscle tissue. Moreover, semaglutide inhibited the amino acid starvation-related stress signaling which was activated under chronic liver injury, resulting in the recovery of mammallian target of rapamycin activity in the skeletal muscle of mice. Second, semaglutide improved skeletal muscle atrophy by directly stimulating GLP-1R in myocytes. Treatment with semaglutide induced cAMP-mediated activation of PKA and AKT, enhanced mitochondrial biogenesis, and reduced ROS accumulation, thereby resulting in inhibition of NF-κB/myostatin-mediated ubiquitin-proteosome degradation and the augmentation of heat-shock factor-1-mediated myogenesis.
Conclusion: Semaglutide may have potential as a new therapeutic strategy for CLD-related skeletal muscle wasting.

Onsite Poster Session 7 [Basic Science & Pathology 3]
P7-3 10061

In Vitro and in Vivo Antitumor Effect of Biofabricated Silver Nanoparticles of Caffeic Acid against Hepatocarcinogenesis by Upregulation of Bax/Bcl2

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Background: Caffeic acid (CFA) is a natural phenolic acid that possesses antitumor activity. The current study was designed to explore the in vitro and in vivo antitumor effect of CFA-mediated biofabricated silver nanoparticles (CFA-AgNPs) against hepatocellular carcinoma (HCC).
Methods: CFA-AgNPs were synthesized by co-precipitation method and characterized by various techniques. Cytotoxic potential of CFA-AgNPs was investigated by MTT assay on HepG2 cells. Subsequently, apoptosis and associated gene expression were determined by using flow cytometry assay and quantitative real-time polymerase chain reaction (qPCR), respectively. HCC was induced in male Sprague Dawley rats by diethylnitrosamine (DEN, 200 mg/kg) administration and CFA-AgNPs were given by oral gavages at two different dose levels (10 and 20mg/kg for 16 weeks). On the last day of study, various antiproliferative parameters were determined.
Result: Characterization techniques confirmed the formation of spherical crystalline CFA-AgNPs with a size range of 50-80 nm and a strong peak of Ag. CFA-AgNPs exhibited significant cytotoxic effects and flow cytometry results revealed stimulation of apoptosis. An increase in p53 and Bax expressions and a reduction in Bcl-2 expression along with upregulation of accompanied Bax/Bcl-2 ratio were observed in qPCR results. In vivo results demonstrated that the CFA-AgNPs administered group significantly downregulated the serum marker hepatic and non-hepatic enzymes and proinflammatory markers.
Conclusion: Results of the current investigation recommended the inhibition potential of CFA-AgNPs against DEN-induced damaging effects on the liver via an antioxidant defense system and modulation of Bax/Bcl2 as well as proinflammatory cytokines.

Onsite Poster Session 7 [Basic Science & Pathology 3]
P7-4 10060

Development and Assessment of a Novel Self Nano Emulsifying Formulation of Furosemide: A Drug Employed in Treating Portal Hypertension

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Background: This research was designed to enhance the water solubility, permeability, and overall bioavailability of furosemide (FURO), a loop diuretic used to manage hypertension in the portal system, by employing a newly developed self nano emulsifying drug delivery system (SNEDDS).
Methods: Solubility analysis of FURO was performed in different oils, surfactants, and co-surfactants. Pseudoternary diagrams were used to identify the self-emulsification range for development of SNEDDS formulations. Various evaluation parameters such as dilution test, droplet size and zeta potential measurement, viscosity, in vitro dissolution efficacy and pharmacodynamic potential of developed formulations were investigated.
Results: In vitro dissolution studies demonstrated a substantial improvement in dissolution rates for the optimized SNEDDS formulation, surpassing both plain FURO and commercially available formulations. The pharmacological effect of FURO was also enhanced when administered through the SNEDDS formulation in comparison to plain FURO.
Conclusion: The current study confirms the potential of SNEDDS formulation as an effective alternative to conventional oral formulations of FURO, offering improved bioavailability and potential benefits for patients.

Onsite Poster Session 8 [Tumor Markers & Biochemistry]
P8-1 10024

Clinical Usefulness of Tumor Markers AFP, L3, and DCP for Treatment of Hepatocellular Carcinoma

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Background and Aim: For obtaining better prognosis in hepatocellular carcinoma (HCC) patients, detecting early stage is important, as possible (Milan criteria: MC-in). Other than alpha-fetoprotein (AFP), fucosylated-AFP (L3) and des-gamma-carboxy-prothrombin (DCP) are also utilized as tumor markers for HCC in Japan. We aimed to evaluate the clinical usefulness of using 3 tumor markers (TMs) in surveillance for detecting MC-in HCC.
Materials/Methods: Of 7563 Japanese HCC patients diagnosed from 2000 to 2019 at our hospitals, 4473 were enrolled after exclusion of major vessel invasion (MVI) and extra-hepatic metastasis (EHM) (median 71 years, HBV:HCV:HBV/HCV:others=574:2577:34:1288). The relationships between tumor burden [sum of maximum tumor diameter (cm) and tumor number] and MC-out with and the 3 TMs (The cut-off values: AFP 20 ng/mL, L3 10% and DCP 40 mAU/mL.) were evaluated, retrospectively.
Results: The median tumor size (maximum) was 4.0 cm, 2878 (64.3%) had single tumor, while MC-out was in 1027 (23%). Among all HCC patients (n=4473), 32.5% were AFP-positive, 39.6% were L3-positive, and 35.4% were DCP-positive. As for MC-in (n=3446), 35.9%, 19.3%, and 44.9% were AFP-, L3-, and DCP-positive, respectively, while 29.2% (n=1008) were AFP negative but positive for at least one of the other two tumor markers. Along with increasing number of positive tumor markers (0, 1, 2, and 3), tumor burden (3.6, 5.1, 5.9, and 9.2, respectively) and percentages of MC-out (6.9%, 20.6%, 27.7%, and 55.9%, respectively) became larger (both $p<0.01$).
Conclusion: Complementary using the 3 TMs for surveillance might increase efficiently detecting chance of MC-in HCC in surveillance.

Onsite Poster Session 8 [Tumor Markers & Biochemistry]
P8-2 10052

Evaluation of Glypican-3 Protein in the Tissues of Hepatocellular Carcinoma by Tissue Microarray

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Among the population of Mongolia, 5,981 new cancer cases were registered in 2021 and 32% of the new cases were hepatocellular carcinoma (HCC). Glypican-3 (GPC3) protein is not expressed in the liver of a healthy person, but it's expression elevated in 70-100% cases of liver cancer. Therefore, we aimed to evaluate GPC3 protein in HCC. In the study, the tumor site and surrounding tissue of a total of 50 participants who were diagnosed with HCC and underwent surgical treatment at the National Cancer Center. GPC3 immunostaining confirmed tissue microarray slides. GPC3 expression were evaluated by the stained proportion of cells and the intensity of staining. A total of 50 participants, 21 men and 29 women, aged 33-79 (average age 64.06±9.1) were included in the study. By tissue microarrays, GPC3 protein was positively stained in 38/50 (76%) of all participants. Of these, 16/38 (42.1%) had weak and 22/38 (57.9%) had strong positive staining. However, when the serum AFP level is normal or less than 20 ng/ml, GPC3 protein is positive in 61.9% (13/21) and when it is greater than 20 ng/ml, 86.2% (25/29) is positive which showed a statistically significant correlation ($p=0.047$). But there was no correlation in other clinical features including age, gender, hepatitis virus infection, tumor size and number, TNM stage and histopathological characteristics with the expression of GPC3 protein ($p>0.05$).GPC3 protein was specifically expressed in the cytoplasm, membrane, and canaliculi of hepatocellular carcinoma. Protein expression was not related to other clinical features and histopathological characteristics.

Onsite Poster Session 8 [Tumor Markers & Biochemistry]
P8-3 10066

Diagnostic Marker of Mitochondrial Dysfunction, AREG, is Associated with Tumor Size in Hepatocellular Carcinoma

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Background and Aim: Many cancer cells adapt to hypoxic conditions and acquire energy production capacity in response to anaerobic respiration, which is less dependent on mitochondrial respiration. Therefore, monitoring mitochondrial dysfunction in hepatocellular carcinoma (HCC) tissue can be an indicator of adaptation to hypoxic environments. However, there are no useful biomarkers of mitochondrial dysfunction in HCC.
Methods: We induced mitochondrial dysfunction by knockdown (KD) of mitochondrial transcription factor A (TFAM), which is essential for the maintenance of mitochondrial DNA in a human hepatoma-derived cell line. Then we performed a comprehensive gene expression analysis. Furthermore, the binding site of the cell stress-responsive transcription factor, c-JUN and the activation site of the enhancer mark by epigenomic analysis were determined by ChIP-seq analysis. To validate the expression levels of the identified candidate genes, RNA extracted from resected HCC specimens was used.
Results: We identified 312 genes overlapped with 1.5-fold increased expression in TFAM-KD, sites of enhancer mark accumulation, and c-JUN binding sites. These included the AREG gene and the CD44 gene. mRNA expression in the resected HCC specimens showed a trend toward increased expression of AREG and CD44 compared to control. Furthermore, AREG gene expression was significantly correlated with tumor diameter in those specimens.
Conclusion: In hepatocellular carcinoma, mitochondrial dysfunction leads to epigenetic remodeling via the transcription factor c-JUN, which is suggested to be involved in the stress response through AREG and CD44 gene expression. The results of this study may contribute to the development of early diagnosis for mitochondrial dysfunction in HCC.

Onsite Poster Session 8 [Tumor Markers & Biochemistry]
P8-4 10002

Andrographolides Regulate c-Myc Stability and Demonstrate Cytotoxic and Genotoxic Activity in CD133+ Multi-drug Resistant Hepatocellular Carcinoma Cells via Small Molecule 20S Proteasome Activation

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Background: c–Myc overexpression, a cancer stem cell (CSC) core marker, promotes malignancy in 70% of human cancers, including hepatocellular carcinoma (HCC). c–Myc is also regulated in a ubiquitin–dependent manner via REGγ activation of the 20S proteasome in addition to the ubiquitin–dependent degradation by 26S proteasome. The activation of small molecule 20S proteasome by andrographolides from Andrographis paniculata – andrographolide (1), 14–deoxyandrographolide (2), 14–deoxy–12–hydroxyandrographolide (3), and neoandrographolide (4) – were demonstrated in CD133+ HepG2 CSCs.
Methods: The cytotoxic activity of compounds 1–4 in HepG2 CSCs was ascertained. This was followed by detection of c–Myc levels via western blot and luminescence assays. RT–qPCR evaluated the expression levels of early apoptotic gene markers, cfos and cjun, including the anti–apoptotic A20. To detect genotoxic activity, single–cell DNA degradation electrophoresis was performed.
Results: Compounds 1–4 decreased c–Myc protein levels in a fashion equivalent to REGγ–mediated c–Myc degradation. Western blot and luminescence assays revealed enhanced levels of c–Myc degradation. HepG2 CSC proliferation was reduced secondary to enhanced apoptotic signaling based on upregulated cfos and cjun expression, with downregulated levels of expressed A20. Genotoxic analysis afforded cometscores (tail length, tail moment, % tail DNA) that were significantly higher compared to vehicle controls. Remarkably, the addition of bortezomib abrogated the effects of 1–4 and reverted to levels similar to vehicle controls. This step confirmed the proteasome–implicated reduction of c–Myc signaling by andrographolides.
Conclusion: These results support the therapeutic potential of small molecule-driven 20S proteasome activation by A. paniculata andrographolides as promising treatments for c–Myc–impelled cancers, especially multi–drug resistant HCC.

Onsite Poster Session 9 [Surgery & Transplantation]
P9-1 10035

Prognosis of the Patients with Multiple Hepatocellular Carcinoma Who Underwent Initial Liver Resection

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Background: We investigated the prognosis of multiple HCC patients underwent liver resection.
Methods: From 2008 to 2019, 258 patients with HCC underwent initial liver resection. The prognosis and prognostic factors were examined by classifying the tumor size and the number of tumors.
Results: There were 180 patients with solitary HCC and 78 patients with multiple HCC. The 5-year recurrence-free survival (RFS) rates for solitary and multiple HCC were 42.9% and 14.2%, and the 5-year overall survival (OS) rates were 82.1% and 69.3%. The prognosis was significantly better in solitary HCC (RFS: P<0.001, OS: P<0.001). In multiple HCC, when divided into maximum tumor diameter of less than 3 cm and 3 cm or more, the 5-year RFS rate was 14.7% and 14.2%, and the 5-year OS rate was 82.0% and 51.4%. There was no significant difference for each. Poor prognostic factors for RFS were partial resection, PIVKA-II over 100mAU/ml, diabetes complications, liver cirrhosis, and 4 or more tumors. Partial resection, diabetic mellitus, and liver cirrhosis were selected as independent RFS factors. The poor prognostic factor for OS was only positive for HCV antigen.
Conclusion: There was no significant difference in the prognosis according to the maximum size of the tumor in multiple HCC. Anatomical resection should be performed if the hepatic function is acceptable.

Onsite Poster Session 9 [Surgery & Transplantation]
P9-2 10113

Impact of Justifying MELD Score Exception by MELD-ALBI Selection on the Outcome of HCC Transplantation

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Background: Hepatocellular carcinoma (HCC) is the most common indication for the model for end– stage liver disease (MELD) exception points; however, its standardization is still challenging due to the conflict of overestimating liver transplantation urgency and the underestimation of the underlying liver function status. We aim to investigate the impact of justifying the MELD exception with Albumin–bilirubin (ALBI) grading on the outcome of HCC transplantation.
Methods: This is a retrospective study investigating patients who had living donor transplantation for HCC from July 2010 to July 2021. Patients were grouped according to MELD score into ≤20 and >20. ALBI grade was calculated and survival was defined from the time of transplantation till death or the last follow–up time.
Results: We identified 64 patients, males (98.4%) with a median age of 48.4 (range (32–63)) years. The median preoperative MELD score was 16 and the median ALBI score was (–1.29). With a cutoff of MELD 20: 3, 5– year survival was (94.3%, 90.9%) for score ≤20 vs (84.6%, 66.6%) for score >20, respectively (p<0.05). Patients graded ALBI-II had better 5– year survival (93.8%) compared to grade III (81.3%) (p>0.05). On combining MELD ≤20 and ALBI grade III; 5– year survival was higher (90%), compared to (61.4%) for MELD >20 and ALBI grade III (p>0.05).
Conclusion: MELD– ALBI selection could optimize liver transplantation urgency mandated by exception points and offer a better evaluation of the underlying liver status for HCC patients.

Onsite Poster Session 9 [Surgery & Transplantation]
P9-3 10092

Usefulness of Laparoscopic Liver Resection for Patients with Ruptured Hepatocellular Carcinoma

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Background: Hepatocellular carcinoma (HCC) is a rupture-prone carcinoma and dissemination is a poor prognostic factor. With advances in interventional radiology (IVR) and anti-tumor drugs, long-term survival of ruptured HCC has become possible. Aim: At our hospital, as a treatment for ruptured HCC, we first perform laparoscopic exploration, and if there are no disseminated lesions, we follow radical laparoscopic liver resection (LLR). If there are no disseminated lesions, sequential LLR is performed. In this presentation, we will demonstrate the technique of LLR for ruptured HCC and examine its safety and usefulness.
Method: Six cases of LLR for ruptured HCC experienced at our hospital since 2019. In this group of cases, the age was 73 (35-83) years, the tumor size was 3.5 (3.0-6.5) cm, the Child-Pugh classification was all A, and the time from rupture to surgery was 62 (58-121) days.
Result: The operative procedures were partial resection in 3 cases and lateral segmentectomy in 3 cases. The operating time was 167 (78-478) minutes, and the blood loss was 150 (0-830) ml. During the observation period of 25.7 (10.7-44.6) months, 1 case of intrahepatic recurrence and 1 case of extrahepatic recurrence (dissemination) were observed, but all of them are alive.
Conclusion: LLR for ruptured HCC is minimally invasive and allows sufficient observation of the peritoneal cavity, making it useful for detecting dissemination and enabling appropriate treatment.

Onsite Poster Session 9 [Surgery & Transplantation]
P9-4 10036

Influence of Child-Pugh B7 and B8/9 Cirrhosis on Laparoscopic Liver Resection for Hepatocellular Carcinoma: A Retrospective Cohort Study

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Background: Laparoscopic liver resection (LLR) for hepatocellular carcinoma (HCC) in patients with Child-Pugh A cirrhosis has been shown to be beneficial. However, less is known regarding the outcomes of such treatment in patients with Child-Pugh B cirrhosis. We conducted a retrospective study to evaluate the outcomes of LLR for HCC in patients with Child-Pugh B cirrhosis, focusing on surgical risks, recurrence, and survival.
Methods: 357 patients with HCC who underwent LLR from 2007 to 2021 were divided into three groups by their Child-Pugh score: the Child-Pugh A (n = 280), Child-Pugh B7 (n = 42), and Child-Pugh B8/9 groups (n = 35). Multivariable Cox regression models for recurrence-free survival (RFS) and overall survival (OS) were constructed with adjustment for preoperative and postoperative clinicopathological factors.
Results: The Child-Pugh B8/9 group had a significantly higher complication rate, but the complication rates were comparable between the Child-Pugh B7 and Child-Pugh A groups (Child-Pugh A vs. B7 vs. B8/9: 8.2% vs. 9.6% vs. 26%, respectively; P = 0.010). Compared with the Child-Pugh A group, the risk-adjusted hazard ratios in the Child-Pugh B7 and B8/9 groups for RFS were 1.39 (0.77-2.50) and 3.15 (1.87-5.31), respectively, and those for OS were 0.60 (0.21-1.73) and 1.80 (0.86-3.74), respectively.
Conclusions: Among patients with HCC, those with Child-Pugh A and B7 cirrhosis can be good candidates for LLR in terms of complications and recurrence. Despite poor postoperative outcomes in patients with Child-Pugh B8/9 cirrhosis, LLR is less likely to interfere with retreatment and can be performed as part of multidisciplinary treatment.

Efficacy and Safeness of Polyglycolic Acid Felt with Fibrin Glue at the Liver Cut Surface for Prevention of Postoperative Bile Leakage in Laparoscopic Liver Resection

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Background: Bile duct injury and bile leakage often occur in extensive liver resection. However, repair of bile duct injury is a complicated technique, especially in laparoscopic liver resection (LLR).This time, we aimed to determine the efficacy of PGA sealant for the prevention of bile leakage after LLR.
Methods: The target is 580 patients who performed LLR from January 2008 to December 2021 at our facility. We started PGA sealant in January 2019.In the PGA group, 1cc fibrin fluid and 1cc thrombin fluid were dropped on the cutting surface. And PGA sheet soaked with 1cc fibrin fluid was stuck on the surface. The PGA was incubated with 1cc thrombin fluid. Finally, fibrin and thrombin were sprinkled over the PGA sheet. From January 2019 to December 2021, 16 patients have been performed PGA methods on LLR. We compared the PGA group with the control group of 28 patients who were background-matched without conventional procedures from January 2016.
Results: No significant difference was observed between the PGA group and the control group in terms of background. In the PGA group, 3 cases were found in intraoperative bile leakage without suturing repair. Postoperative bile leakage occurred in 2 patients in the control group. In the PGA group, postoperative hospital stay was 7.5 (5-21) days shorter than in the control group.
Conclusion: Polyglycolic acid felt sealant with fibrin glue at the liver cut surface in LLR is easy to handle and safe. This technique may suppress postoperative bile leakage.

Onsite Poster Session 10 [Liver Cirrhosis & Sarcopenia]
P10-1 10037

VWF/ADAMTS13 Ratio as a Potential Predictive Biomarker for Acute Kidney Injury Onset in Cirrhosis

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Background: We aimed to investigate the von Willebrand factor to ADAMTS13 ratio (VWF: Ag/ADAMTS13:AC) as a potential biomarker for acute kidney injury (AKI) outcomes in patients with liver cirrhosis (LC).
Method: The observational study included patients with LC who developed AKI (AKI group: n=91) and patients with LC who did not developed AKI [non-AKI (NAKI) group, n=91], as a control group. Plasma levels of von Willebrand factor antigen (von Willebrand factor: Ag) and ADAMTS13 activity (ADAMTS13:AC), were measured in patients with both AKI and NAKI. The risk factors for the development, 90-day mortality and poor treatment response of AKI were identified.
Results: AKI group had a significantly higher VWF:Ag/ADAMTS13:AC than NAKI group. Values 5.7 or higher of VWF:Ag/ADAMTS13:AC were identified as an independent factor for AKI development in patients with LC (hazard ratio [HR], 2.56; 95% CI, 1.26-4.99; p&lt0.001). Among the patients with AKI, values 9.0 or higher of VWF:Ag/ADAMTS13:AC were identified as an independent factor for 90-day mortality (HR 6.83; 95% CI, 2.32-20.10; p&lt0.001). Cumulative survival was significantly lower in those with 9.0 or higher versus low (&lt9.0) VWF:Ag/ADAMTS13:AC. Furthermore, values 7.4 or higher of VWF: Ag/ADAMTS13:AC were identified as an independent factor for poor treatment response (HR 4.2; 95% CI, 1.39-12.70; p&lt0.001). The response rates of treatment were significantly higher in those with low (&lt7.4) VWF:Ag/ADAMTS13:AC than in those with 7.4 or higher of VWF:Ag/ADAMTS13:AC.
Conclusion: VWF:Ag/ADAMTS13:AC potentially predicts development and prognosis and treatment response of AKI in patients with LC.

Onsite Poster Session 10 [Liver Cirrhosis & Sarcopenia]
P10-2 10040

Diagnostic Markers for Portal Vein Thrombosis in Patients with Cirrhosis PVT

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Background and Aims: Portal vein thrombosis (PVT) is one of the most common hepatic vascular disorders associated significant morbidity and mortality. A disintegrin-like and metalloproteinase with thrombospondin type-1 motifs 13 (ADAMTS13) specifically cleaves multimeric von Willebrand factor (VWF) thereby controls VWF-mediated platelet thrombus formation. An imbalance between ADAMTS13 and VWF is responsible for hypercoagulability, including spontaneous thrombus formation in blood vessels. We aimed to identify diagnistic markers for PVT in patients with cirrhosis.
Methods: 66 patients with cirrhosis were split into two group: PVT groups (n=33) and non PVT (NPVT) group (n=33). Plasm ADAMTS13 activity (ADAMTS13:AC) and VWF antigen (VWF:Ag) were measured using enzyme-linked immunosorbent assays at diagosis of PVT in PVT group.
Results: Plasm ADAMTS13:AC was significantly higher in NPVT group than in PVT group, whereas no significant differences in plasma VWF:Ag were observed in patients with cirrhosis. ADAMTS13:AC was an independent risk factor for developing PVT on multivariate (Odds ratio [OR] = 0.00694, 95% confidence interval [95%CI]: 0.000786-0.0613, p < 0.001) as a risk factor of PVT. The Receiver operating characteristic analysis for PVT revealed a good classifying capability, with an AUC of 0.913. Patients having ADAMTS13:AC of greater than or equal to 20 had a higher incidence of PVT versus ADAMTS13:AC below 20.0.
Conclusion: Serum ADAMTS13:AC can serve as diagnostic maker for PVT in patients with cirrhosis.

Onsite Poster Session 10 [Liver Cirrhosis & Sarcopenia]
P10-3 10004

The Geriatric Nutritional Risk Index is a Useful Predictor of Muscle Volume Loss Regardless of Gender

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Background: Muscle volume loss (pre-sarcopenia) is a crucial factor affecting the prognosis of patients with chronic liver disease (CLD) and hepatocellular carcinoma (HCC). An easily applicable and predictive tool is needed. This study aimed to investigate the clinical usefulness of the geriatric nutritional risk index (GNRI), which utilizes serum albumin, height, and body weight, in identifying high-risk CLD patients for pre-sarcopenia.
Methods: From 2017 to 2022, 442 HCC patients with CT data, who had no past history of treatments, were included (72.6% male, median age 74 years, Child-Pugh A:B:C=357:67:18). The GNRI was used to assess nutritional status, and pre-sarcopenia was evaluated using the skeletal muscle index cut-off value of the Japan Society of Hepatology. The relationship between GNRI and pre-sarcopenia was assessed retrospectively.
Results: Pre-sarcopenia was found in 105 (23.8%). The cut-off GNRI score for predicting pre-sarcopenia was 99.7 (specificity/sensitivity=0.730/0.795) (AUC 0.824, 95% CI: 0.771-0.878) in males, and 99.4 (specificity/sensitivity=0.685/0.781) (AUC 0.782, 95% CI: 0.689-0.876) in females. The cut-off GNRI score for pre-sarcopenia in all patients was 99.7 (specificity/sensitivity=0.709/0.800) (AUC 0.813, 95% CI: 0.766-0.859), which was approximately the upper limit of mild nutritional decline status. Furthermore, also after excluding patients with ascites, the cut-off GNRI score for pre-sarcopenia was 99.7 (specificity/sensitivity=0.760/0.744) (AUC 0.803, 95% CI: 0.747-0.858).
Conclusions: The GNRI provides a simple and effective tool for predicting pre-sarcopenia in CLD patients. Nutritional intervention is crucial to maintain a normal GNRI score, and muscle volume should be assessed in patients with an abnormal score.

Onsite Poster Session 10 [Liver Cirrhosis & Sarcopenia]
P10-4 10131

Coexistence of Muscle Atrophy and High Subcutaneous Adipose Tissue Predicts Poor Prognosis in Hepatocellular Carcinoma

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Purpose: We aimed to assess the prognostic implications of muscle atrophy (MA) and high subcutaneous adipose tissue (SAT) in patients with hepatocellular carcinoma (HCC).
Methods: In this retrospective study, MA was assessed using the psoas muscle index (PMI) obtained from computed tomography. SAT was evaluated based on radiodensity measurements. Survival and multivariate analyses were performed to identify factors associated with prognosis. The impact of MA and high SAT on prognosis was determined through survival analysis.
Results: A total of 201 patients (median age: 71 years; 76.6% male) with HCC were included. Liver cirrhosis was observed in 72.6% of patients, and the predominant Child Pugh grade was A (77.1%). A total of 33.3% of patients exhibited MA based on PMI values, while 12.9% had high SAT radiodensity. Kaplan Meier survival analysis demonstrated that patients with MA had significantly poorer prognosis than those without MA. Patients with high SAT had a significantly worse prognosis than those without it. MA, high SAT, BCLC class B, C, or D, and Child Pugh score >5 were significantly associated with overall survival. Further classification of patients into four groups based on the presence or absence of MA and high SAT revealed that patients with both MA and high SAT had the poorest prognosis.
Conclusion: Our findings highlight the importance of evaluating both MA and high SAT as prognostic factors in patients with HCC. Identifying this high-risk subgroup may facilitate the implementation of targeted interventions, including nutritional therapy and exercise, to potentially improve clinical outcomes.

Onsite Poster Session 11 [Hepatitis C, Hepatitis B]
P11-1 10103

High HBV DNA Level Increase the Risk of Tumor Recurrence after Surgical Resection or Ablative Therapy in Patients with HBV Related Hepatocellular Carcinoma

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The recurrence rate of hepatocellular carcinoma (HCC) is considerably high even in patients who underwent surgical resection or ablative therapy which are regarded as a curative modality. Although various factors have been reported as risk factors of the tumor recurrence, there is little report for the influence of viral status on tumor recurrence in patients with hepatitis B virus (HBV) related HCC. Hence, we investigated that the role of HBV DNA level about tumor recurrence in patients with HBV related HCC. We retrospectively analyzed 106 patients who had HBV related HCC and underwent surgical resection (n= 67) or ablative therapy (n=39) for curative purpose. The value of high HBV DNA level was defined as more than 2.8 x 10 5 copies/mL. Overall, 30 of 106 patients (35.8%) developed a tumor recurrence during the follow-up period (31.0-43.7 month). Fifty eight patients (56.3%) had high baseline HBV DNA level. Recurrence free survival rate in patients with high HBV DNA level was significantly lower than that of the others (35.9 vs 56.5 months, p=0.001). HBeAg positivity (p=0.001) and Child-Pugh class B (p=0.04) were also correlated with tumor recurrence. In multivariate analysis, high HBV DNA level (p=0.001) and Child-Pugh class B (p=0.013) were identified as independent risk factors for tumor recurrence. High HBV DNA level increase the risk of tumor recurrence even in patients with HBV-related HCC who underwent surgical resection or ablative therapy. Large prospective study whether antiviral therapy to suppress HBV DNA level could decrease the tumor recurrence is needed.

Onsite Poster Session 11 [Hepatitis C, Hepatitis B]
P11-2 10020

Four-year Safety and Effectiveness of Tenofovir Alafenamide in Treatment-experienced Patients with Chronic Hepatitis B

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Background: Switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) improves outcomes for patients with chronic hepatitis B (CHB); however, long-term real-world data are limited. The aim of this study was to assess the safety and effectiveness for treatment-experienced CHB patients treated with TAF for up to four years.
Methods: This multicenter, retrospective cohort study consisted of adult CHB patients who switched to TAF 25mg. Primary outcomes were viral suppression (VR: HBV DNA&It;10 IU/mL), ALT normalization (BR: ALT&It;35/25 U/L men/women), and complete response (CR: viral plus biochemical response) within four years. Safety assessment included changes in estimated glomerular filtration rate (eGFR).
Results: We enrolled 463 eligible patients. The mean age was 57.9±12.6, and 14.9% had cirrhosis. All had been treated with entecavir (n=200), TDF (n=135), or a combination of nucleos(t)ide analogues (n=128). Sixty-five (14.0%) had HBV DNA>20 IU/mL at baseline. In the four-year follow-up, the proportions of VR and BR increased, to 95.7%/81.1%, 96.3%/80.9%, 97.8%/83.2%, 97.8%/82.1%, and 98.9%/83.5% at month 6, year 1, year 2, year 3, and year 4, respectively. Likewise, the proportions of CR also significantly increased, to 81.4%, 81.4%, 83.8%, 82.7%, and 84.6% (P&It;0.01, compared to baseline). For patients who switched from a TDF-containing regimen to TAF, eGFR significantly improved during the first 6 months (+3.1 mL/min/1.73m2) (P&It;0.01).
Conclusion: TAF had a potent virological and biochemical effect for treatment-experienced patients with CHB. Moreover, patients who switched from TDF to TAF can benefit from TAF therapy in terms of improvement of renal function.

Onsite Poster Session 11 [Hepatitis C, Hepatitis B]
P11-3 10123

The Genotypic Association of Hepatitis C Associated Oral Lichen Planus and its Response to Direct Acting Antivirals- A Case Series

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Objectives: Oral Lichen Planus (OLP) is one of the extraneous manifestation of hepatitis C infection. Various genotypes may be associated with OLP. The genotypes vary in pathogenicity and response to direct-acting antivirals (DAAs). The study was done to assess the various genotypes linked with hepatitis C associated OLP.
Methods: Lichen Planus refractory to conventional steroid treatment was considered as an oral manifestation of HCV and it was confirmed by anti-HCV by ELISA (third generation). Genotyping was done using genotype specific core primers in nested polymerase chain reaction, NS5B sequencing and 5' non coding region based PCR restriction fragment length polymorphism. Patients with HCV-related OLP received Sofosbuvir with ribavirin for 24 weeks. OThe patient response were assessed before and after treatment using escudier scoring system.
Results: Most common genotype associated with OLP was 3(65%) followed by 1(25%) and 4(15%).In our sample the other genotypes were not seen. Sustained virological response was observed in all patients irrespective of the genotype OLP was associated with. There was no worsening of lichen planus in any of the treated patients. Clinically refractory lichen planus resolved with DAAs treatment.
Conclusion: HCV associated OLP responded to DDAs irrespective of the genotype corresponding to a reduction in escudier score.

Onsite Poster Session 11 [Hepatitis C, Hepatitis B]
P11-4 10034

Directly Acting Antivirals Improve Insulin Resistance in Non-diabetic Patients with Hepatitis C: A Meta-analysis

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Background: Insulin resistance, beta-cell dysfunction, and diabetes mellitus (DM) are the extrahepatic complications of chronic hepatitis C virus (HCV) infection. The aim of the study was to determine the effects of novel directly acting antivirals (DAA) on insulin resistance and insulin sensitivity parameters in non-diabetic patients with HCV infection.
Methods: A systematic search of Pubmed, Scopus, and Google Scholar was conducted for studies published until May 1, 2023. Studies investigating the effect of any DAA on insulin resistance and insulin sensitivity parameters in non-diabetic chronic HCV patients with sustained virologic response were included. The primary outcome assessed was the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR). The pooled outcomes were compared pre-and post-treatment with DAAs using Hedges' g (HG) with a 95% confidence interval (CI).
Results: A total of eight studies were included in the meta-analysis. Insulin resistance measured by the HOMA-IR was significantly reduced with DAA therapy (HG = 1.00, 95% CI: 0.52-1.47, $p<0.001$). A similar significant reduction in fasting insulin levels was observed following DAA therapy (HG = 0.96, 95% CI: 0.54-1.38, $p<0.001$). However, no significant differences were seen in Homeostasis model assessment for insulin sensitivity (HOMA-S) (HG = 0.02, 95% CI: -0.82-0.86, $p = 0.96$), and the homeostasis model assessment of beta-cell function (HOMA-B) (HG = -0.06, 95% CI: -0.41-0.29, $p = 0.73$) before and after DAAs use.
Conclusions: The use of DAAs in non-diabetic chronic HCV patients with a sustained virologic response also significantly reduces insulin resistance and fasting insulin levels.

Onsite Poster Session 12 [Hepatitis C]
P12-1 10095

A Novel Formula Used for Predicting Hepatocellular Carcinoma after the Achievement of SVR by DAAs in Patients with Chronic Hepatitis C

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Previously, we developed a new formula to predict advanced liver fibrosis. This study aimed to clarify the usefulness of this formula for predicting HCC after achieving SVR. New formula scores were used as a marker for predicting liver fibrosis and as a predictive model for HCC incidence. The participants were 172 men and 127 women with a median age of 68 years. The cumulative HCC incidence rates were 4.3%, 9.7%, and 12.5% at 1, 3, and 5 years, respectively. Multivariate analysis revealed that male sex (P = 0.021) and high new formula scores (P = 9.40×10-4) were independent factors associated with the development of HCC in patients without a treatment history of HCC. The optimal cutoff value for predicting the development of HCC was -0.214. The cumulative incidence rates of HCC in patients with new formula scores ≥ -0.214 were 5.4%, 15.3%, and 15.3% at 1, 3, and 5 years, respectively, whereas the incidence rates of HCC in patients with new formula scores < -0.214 were 0.0%, 0.6%, and 4.8%, respectively (P = 2.12×10-4). In conclusion, this study demonstrated the usefulness of new formula scores as a predictor of HCC after achieving SVR, especially in patients without a history of treatment for HCC.

Onsite Poster Session 12 [Hepatitis C]
P12-2 10074

Hepatic Steatosis is a Risk Factor for All-organ Carcinogenesis in Post-SVR Patients

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Purpose: To determine the relationship between fat, fibrosis and carcinogenesis in a cohort of prospective studies after SVR.
Methods: A prospective study of 651 SVR cases were conducted from July 2013 to December 2021. The primary endpoint was the occurrence of all malignancies. Patients were divided into 4 groups based on pretreatment Fibro-scan VCTE 15.4 kPa and CAP 229 dB/m (group A; low fiber/low fat, group B; high fiber/low fat, group C; low fiber/high fat, group D; high fiber/high fat). The carcinogenic rate during the follow-up period was calculated using the person-year method.
Results: The median observation period was 5.44 years. During the observation, 107 malignancies occurred in 99 patients. The incidence rate of all malignancies was 3.68/100 person-years. The cumulative incidence was 3.4% for 1 year, 11.0% for 3 years, and 17.5% for 5 years, and continued to increase almost linearly. 334/88/178/51 patients were in groups A/B/C/D, respectively. HCC incidence was 1.01/4.88/1.37/6.10 /100 person-years. The carcinogenic rate increased 5-fold with increasing fibrosis and 1.3-fold with increasing steatosis. The incidence of cancer of other organs was 1.48/0.96/2.61/2.91/100 person-years. The carcinogenic rate was almost the same with higher fibrosis, but the carcinogenic rate increased more than 2-fold with higher steatosis. During observation, liver fibrosis showed a trend toward remission, while f steatosis showed a trend toward worsening.
Conclusion: Hepatic steatosis in patients after SVR was 1.3 times higher in HCC and more than 2 times higher in cancer of other organs.

Onsite Poster Session 12 [Hepatitis C]
P12-3 10082

Surveillance should Continue after SVR -Carcinogenesis Continues to Increase in a Linear Fashion-

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Background: Achieving SVR does not completely eliminate the risk of liver cancer, and ongoing liver cancer surveillance is recommended. However, it is not clear how long patients should be followed. Furthermore, the incidence of all organ malignancies other than liver cancer has not been elucidated.
Purpose: Reconsider the need for surveillance by analyzing all carcinomas (liver + other organs) in cases where SVR was obtained.
Methods: A prospective study of 651 SVR cases was conducted from July 2013 to December 2021. The primary endpoint was the occurrence of all malignancies, and the secondary endpoint was overall survival.
Results: The 651 patients who achieved SVR were prospectively observed until December 2021. The overall median observation period was 5.44 years. During follow-up, 107 malignancies occurred in 99 patients. The incidence of all malignancies was 3.68/100 person-years. The cumulative incidence was 3.4% at 1 year, 11.0% at 3 years, and 17.5% at 5 years, and continued to increase almost linearly. Of the 651 patients, 32 died during the follow-up period: 1-year survival rate was 99.2%, 3-year survival rate was 96.3%, and 5-year survival rate was 94.2%.
Conclusion: A prospective study of overall malignancy development and overall survival in patients who achieved SVR found that malignancies of other organs continued to develop at the same rate as hepatocellular carcinoma. The incidence of all malignancies continued to increase almost linearly that suggesting the need for continued surveillance in patients after SVR.

Onsite Poster Session 12 [Hepatitis C]
P12-4 10084

Continued Surveillance after SVR Yields a Prognosis Equivalent to the Standardized Mortality Ratio (SMR)

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Background: Achieving SVR does not completely eliminate the risk of liver cancer, and ongoing liver cancer surveillance is recommended. However, it is not clear how long patients should be followed. Furthermore, the incidence of all organ malignancies other than liver cancer has not been elucidated.
Purpose: To examine whether continued surveillance of cases with SVR contributes to improved life expectancy.
Methods: A prospective study of 651 SVR cases was conducted from July 2013 to December 2021. The primary endpoint was the occurrence of all malignancies, and the secondary endpoint was overall survival. For overall survival, survival rates were calculated for all eligible patients. Sex- and age-matched SMRs were used for comparison with the general population.
Results: The 651 patients who achieved SVR were prospectively observed until December 2021. The overall median observation period was 5.44 years. During follow-up, 107 malignancies occurred in 99 patients. The incidence of all malignancies was 3.68/100 person-years. Of the 651 patients, 32 died during the follow-up period: 1-year survival rate was 99.2%, 3-year survival rate was 96.3%, and 5-year survival rate was 94.2%. Overall survival after SVR was not significantly different but was higher than SMR (98.7% at 1 year, 95.8% at 3 years, and 92.5% at 5 years).
Conclusion: A prospective study of patients who achieved SVR found that other organ malignancies continued to occur as frequently as HCC. However, with continued surveillance, patients after SVR have a prognosis comparable to that of SMR.

Onsite Poster Session 13 [NASH/ NAFLD & Genetic/ Metabolic Disease]
P13-1 10039

Favorable Liver and Skeletal Muscle Changes in Patients with NAFLD and Type 2 Diabetes Receiving GLP-1 Receptor Agonist

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Background and Aims: The aim of this study was to investigate changes in obesity severity, glucose and fat metabolism, skeletal muscle, and liver in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM).
Methods: Twenty-one patients with NAFLD who received the glucagon-like peptide 1 receptor agonist semaglutide for T2DM were included. Body weight (BW), metabolic parameters, liver enzymes, fibrosis markers, skeletal muscle area (cm2), and its fat fraction (%) at the L3 level using the two-point Dixon method on MRI, as well as liver steatosis and liver stiffness assessed by MRI-PDFF and MR elastography, respectively, were prospectively examined before and 6 months after semaglutide administration.
Results: The mean age was 53 years, and 47.6% were female. Skeletal muscle fat fraction significantly increased with age (r=0.51, p=0.0184) on baseline MRI. Conversely, liver fat fraction decreased with age on baseline MRI. Semaglutide dramatically reduced hemoglobin A1c (%) (6.8 vs. 5.8; p=0.0003), AST (IU/L) (54 vs. 26, p<0.0001), ALT (IU/L) (80 vs. 34, p=.0004), γ-GTP (IU/L) (64 vs. 34, p=0.0007), and liver fat fraction (%) (22 vs. 12, p=0.0014). Although not statistically significant, BW (kg) (79.9 vs. 77.4), body mass index (BMI) (kg/m2) (28.9 vs. 27.6), liver stiffness (kPa) (28.9 vs. 27.6), and skeletal muscle fat fraction (%) (28.9 vs. 27.6) showed a decreasing trend.
Conclusion: Skeletal muscle steatosis significantly increased in elderly patients with NAFLD and T2DM. Semaglutide demonstrated a favorable effect on both liver and skeletal muscle steatosis, leading to improved liver function and diabetic status.

Onsite Poster Session 13 [NASH/ NAFLD & Genetic/ Metabolic Disease]
P13-2 10043

Effects of SGLT2 Inhibitors on Liver Steatosis and Fibrosis in Non-alcoholic Fatty Liver Disease and Type 2 Diabetes: A Meta-analysis

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Background: The aim of the study was to determine the effects of sodium-glucose cotransporter 2 inhibitors (SGLT2i) on liver steatosis reduction and liver fibrosis regression in non-alcoholic fatty liver disease (NAFLD) patients with type 2 diabetes mellitus (T2DM).
Methods: A systematic search of medical databases was conducted for studies published until April 2023 in the English language. Studies investigating the effect of any SGLT2i on any one of the parameters of liver steatosis and liver fibrosis in NAFLD patients with T2DM were included. The pooled outcomes were compared pre-and post-treatment with SGLT2i using Hedges' g (HG) with a 95% confidence interval (CI).
Results: A total of 18 studies were included in the meta-analysis. Hepatic steatosis measured with continuous attenuation parameter (CAP) was significantly reduced with SGLT2i therapy (HG = 0.76, 95% CI: 0.22-1.29, p = 0.01). A similar significant reduction in hepatic steatosis was observed in MRI-proton density fat fraction% (HG = 0.77, 95% CI: 0.42-1.13, p<0.001). A significant hepatic fibrosis regression was found following SGT2i use when measured with Fibroscan (HG = 0.36, 95% CI: 0.04-0.68, p = 0.03). The FIB-4 Index decreased (HG = 0.18, 95% CI: 0.06-0.30, p<0.001) and the levels of type IV collagen 7S declined (HG = 0.52, 95% CI: 0.28-0.76, p<0.001) with the use of SGLT2i.
Conclusion: Use of SGLT2i in patients with NAFLD and T2DM significantly reduces hepatic steatosis and hepatic fibrosis.

Onsite Poster Session 13 [NASH/ NAFLD & Genetic/ Metabolic Disease]
P13-3 10079

Effects of Lanifibranor on High-Fat Diet-Induced-Nonalcoholic Fatty Liver Disease and Associated Mood Disorder in Mice

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Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease and causes liver"-"related mortality. NAFLD is associated with systemic metabolic diseases, including obesity and diabetes. NAFLD patient also has a higher prevalence of depression and anxiety. Lanifibranor is a pan"-"peroxisome proliferator"-"activated receptor agonist, which has been proven to have anti-fibrotic and anti"-"inflammatory effects; however, its effect on NAFLD"-"related mood disorder is still unclear. In this study, we investigated the effects of a Lanifibranor on high"-"fat diet"-"induced NAFLD and mood disorder in mice. The mice were fed a 45% high"-"fat diet with or without lanifibranor injection. Administration of Lanifibranor significantly reduced serum levels of ALT, LDL, fatty acid, and triglyceride in mice. Liver histological images showed fewer fat vacuoles in mice treated with Lanifibranor. Moreover, Lanifibranor can effectively decrease liver fatty acid and triglyceride levels by inhibiting lipogenesis. Additionally, high"-"fat diet"-"induced adipose tissue enlargement was inhibited by Lanifibranor treatment. Consumption of high"-"fat"-"diet induced anxiety"-"like and depression"-"like behaviors in mice. Lanifibranor treated group slightly improved depression"-"like behavior, but has no effect in anxiety"-"like behavior. In conclusion, our study showed that Lanifibranor treatment decreases lipid accumulation in the liver, fat storage in the adipose tissue and depression"-"like behavior in high"-"fat diet fed mice.

Onsite Poster Session 13 [NASH/ NAFLD & Genetic/ Metabolic Disease]
P13-4 10025

Vitamin D Deficiency Exacerbates Alcohol-related Liver Injury via Gut Barrier Disruptionand Hepatic Overload of Endotoxin

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Background: Endogenous lipopolysaccharide (LPS) that is translocated via the disrupted intestinal barrier plays an essential role in the progression of alcohol-related liver disease (ALD). Vitamin D deficiency is observed in ALD, and it participates in regulating gut barrier function. Therefore, we investigated that the impact of vitamin D deficiency on ethanol (EtOH)- and carbon tetrachloride (CCl4)-induced liver injury relevant to gut barrier disruption in mice.
Methods: To investigate the hypothesis, we fed female C57BL/6J mice a liquid diet containing 2.5% EtOH and intraperitoneal injections of CCl4 twice weekly for 8 weeks. The mice were divided into vitamin D-deficient (vitamin D: 1.6 IU/kg) and vitamin D-sufficient (vitamin D: 54.4 IU/kg) groups. In addition, we cultured CaCo2 cells to examine the direct effects of vitamin D on intestinal cells.
Results: The EtOH/CCl4-treated mice developed hepatic steatosis, inflammation, and fibrosis, which were significantly exacerbated by vitamin D-deficient diet. Vitamin D deficiency enhanced gut hyperpermeability by reducing the intestinal expressions of tight junction proteins including ZO-1, occludin, and claudin-2/5/12/15 in the EtOH/CCl4-treated mice. Consequently, it induced Kupffer cell infiltration and LPS/toll-like receptor 4 signaling-mediated proinflammatory response in the liver. Based on the in vitro assay, vitamin D3-mediated vitamin D receptor activation inhibited EtOH-stimulated paracellular permeability and the downregulation of tight junction proteins in Caco-2 cells.
Conclusion: Vitamin D deficiency exacerbates alcohol-related liver injury via gut barrier disruption and hepatic overload of endotoxin.

Onsite Poster Session 14 [Others 1]
P14-1 10047

Clinical Features Related to the Prognosis of Patients with Ruptured Hepatocellular Carcinoma as Initial Symptom

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Background/Aim: Although rupture of hepatocellular carcinoma (HCC) is known to be a poor prognostic factor, some affected patients have a good prognosis. This study aimed to elucidate the clinical features of patients with ruptured HCC and a better prognosis.
Materials/Methods: From 1998 to 2022, 75 HCC patients with rupture as an initial symptom were enrolled (median age 71 years, Child-Pugh classification A:B:C = 30:36:9). Death within 3 months after HCC rupture was defined as the short mortality (SM) group (study-1), and survival over 1 year was defined as the long survival (LS) group(study-2). Clinical features were evaluated retrospectively according to each definition.
Results: In study-1, the SM group showed poorer hepatic reserve function than the others (Child-Pugh classification A:B:C = 6:12:9 vs. 24:24:0, ALBI score -1.82 vs. -2.16, $p<0.01$ for each). The wait-and-see surgical resection rate in the SM group was lower than the others (18.5% vs. 58.3%, $p<0.01$). In study-2, the LS group showed better hepatic reserve function [Child-Pugh classification A:B:C = 17:14:0 vs. 13:22:9, $p<0.01$), ALBI score (-2.26 vs. -1.85, $p=0.01$)], smaller tumor diameter (6.0 cm vs. 9.1 cm, $p<0.01$) than the others. The overall survival of all patients who received radical surgery was significantly better than those who did not (median 55.2 months vs. 13.2 months, $p<0.01$).
Conclusion: Even in patients with ruptured HCC, preserved liver reserve and relatively small tumor size are thought to be important prognostic factors. If surgical resection challenge is possible in such affected patients, a favorable prognosis might be expected.

Onsite Poster Session 14 [Others 1]
P14-2 10070

The Clinical Results of Switching from Zoledronic Acid Hydrate to Denosumab for Bone Metastasis of Hepatocellular Carcinoma, Single-center Simple Open-labeled Prospective Interventional Trial

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Background: The zoledronic acid hydrate (ZOL) reduces the risk associated with bone metastasis. The denosumab has revealed as a better option for bone metastasis. But few studies reported about the denosumab for bone metastasis of hepatocellular carcinoma (HCC). We prospectively assessed the clinical outcome of switching from ZOL to denosumab for bone metastasis of HCC.
Method: Ten HCC patients with bone metastasis were enrolled and illegible in this prospective study. They remained abnormal level of type 1 collagen cross-linked N-telopeptide (NTx) or growth of tumor even though administered ZOL over three months. We switched from ZOL to 120 mg of denosumab every four weeks and check out the clinical outcomes on the point of every administration, such as the change of NTx, the answer for a questionnaire about pain, ADL disturbance, and adverse events.
Result: All case of the urine NTx clearance were normal. The average of urine NTx clearance changed from 13.2 to 21.2 nmol BCE/nmol·Cre ($p=0.54$). Then, all case of the serum NTx kept abnormal range. The average changed 142 to 126 nmol BCE/nmol ($p=0.56$). The answer for the questionnaire about the pain and ADL did not change significantly. Some patients showed the elevation of transaminases, but not owing to the change of drug.
Conclusion: Switching to denosumab from ZOL for bone metastasis of HCC did not change pain score and ADL during the terminal periods.

Health Related Quality of Life of Hepatocellular Carcinoma Metastasis to Oral Cavity -A Systematic Review

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Dexton Johns

Hepatocellular carcinoma (HCC) is a rare entity in the oral cavity. Just 41 cases have been reported in the scientific literature. Among the oral carcinomas only 1% accounts from liver metastasis. Oral metastasis occurs only in the advanced stages of HCC and the treatment is usually palliative.

Objective: To assess the physical and mental health related quality of life (HRQoL) after diagnosing oral manifestation of HCC.

Methods: A systematic review and meta-synthesis techniques were adopted to identify, appraise and synthesize the relevant literature regarding the experience of HCV patients conducted according to the PRISMA guidelines. Several electronic databases such as PubMed, CINAHL, Scopus, PsycINFO and the Cochrane Library databases were searched.

Results: There was male predilection and the mean survival was 19 months. The patients were in late 50 or early 60 when diagnosed with the oral changes. HRQOL had a statistically significant correlation with age, sex, educational level, living type, employment status, monthly income level, and comorbidity status. The symptoms reported include pain, swelling, numbness, halitosis, bleeding from gums and mobility of tooth. There was increased involvement in maxilla.

Conclusions: Education, compassion and health care needs to be tailored to improve the overall well-being of patients with HCV. The prognosis is poor in oral HCC manifestation so both a mental and physical support are pivotal in the quality of life during the end stages.

Onsite Poster Session 15 [Others 2]
P15-1 10055

Long-Term Outcomes and Incidence of Hepatocellular Carcinoma in Primary Biliary Cholangitis Complicated with CREST Syndrome

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Aim: Although there have been some reports of primary biliary cholangitis (PBC) complicated by CREST syndrome (PBC-C), the long-term prognosis of these patients has not been fully investigated. Herein, the long-term prognosis of PBC-C was compared with that of PBC alone.
Methods: The study included 302 patients diagnosed with PBC at our hospital from December 1990 to August 2021. The survival rates of patients who did not undergo liver transplantation (LT) were compared between those who had PBC-C (n=57) and those who had PBC alone (n=245). Moreover, 173 patients were divided into two groups (PBC-C (n=26) and PBC alone (n=147)), and GLOBE and UK-PBC scores were compared. CREST syndrome diagnosis was based on anti-centromere antibody positivity and the presence of at least 2 of the 5 clinical CREST symptoms.
Results: The median observation period was 5.4 years. Six patients developed hepatocellular carcinoma (HCC), and the patients with PBC-C had fewer HCC cases than the patients with PBC alone. The survival rates without LT (3/5/10 years) were 98/96/96% for the PBC-C and 92/87/80% for the PBC-alone, with a significantly better prognosis in the PBC-C (log-rank, P=0.0172). The predicted liver-related death and LT risk (5/10/15 years) was significantly lower in the PBC-C (2.4/7.6/13.2%) than in the PBC-alone (4.8/11.8/18.8%; P&lt0.05). The predicted LT-free survival (3/5 years) was significantly higher in the PBC-C (93/88%) than in the PBC-alone (88/81; P&lt0.05).
Conclusion: PBC-C may have a better long-term prognosis than PBC alone.

Onsite Poster Session 15 [Others 2]
P15-2 10007

Prediction of Recurrence after Curative Treatment for Hepatocellular Carcinoma Using aMAP Risk Score

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Background/Aim: This study aimed to evaluate the utility of the aMAP score, a predictive tool for assessing the risk of hepatocellular carcinoma (HCC) with chronic hepatitis, in predicting the initial recurrence of HCC in patients who underwent curative treatment.
Materials/Methods: A total of 1021 patients with HCC within the Milan criteria treated between January 2000 and August 2022 were enrolled. The cohort was divided into two groups based on their aMAP scores (High≥60, Low<60) and compared for recurrence-free survival (RFS) and overall survival (OS).
Results: The Low and High groups were significantly different in terms of etiology (HBV:HCV:HBV+HCV:NBNC=41:80:2:37 vs. 65:589:11:196, p=0.044), AST (46 vs. 40 IU/L, p<0.001), and multiple HCC (14% vs. 22%, p=0.021). Median RFS (59.8 vs. 30.9 months; p<0.001) and median OS (151.9 vs. 82.2 months, p<0.01) were significantly better in the Low group. In patients with HCC due to chronic viral hepatitis, the difference in RFS between the Low and High groups was significant (59.8 vs. 30.6 months, p<0.001), particularly for HCV-positive patients (53.1 vs. 27.2 months, p=0.002). However, in non-viral patients with HCC, there was no significant difference in RFS between the High (32.0 months) and Low (70.9 months) groups.
Conclusion: This retrospective study indicates that elevated aMAP scores are significantly associated with worse RFS in patients with HCC caused by chronic viral hepatitis, particularly those with HCV. The aMAP score is a useful tool for assessing the risk of recurrence following curative treatment.

Onsite Poster Session 15 [Others 2]
P15-3 10133

Journey and Evolution of Comprehensive Genomic Analysis: Integrating Panel Sequencing to Expert Panel Implementation

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Yamanashi Central Hospital established its Genomic Analysis Center in 2013 to promote genomic analysis and precision medicine. Over the years, the center has conducted a variety of in-house panel sequencing analyses, including gastrointestinal, lung, breast, gynecological, urological, familial cancers and BRCA1/2 analyses using clinical samples. These analyses have helped elucidate the genetic basis of tumorigenesis, tumor progression and drug resistance. To enhance patient services, the hospital has also integrated insurance-covered genetic testing, such as the Oncomine DX test, RAS/BRAF and MSI testing in the Department of Genetics and Clinical Laboratory, into its clinical practice.
In recognition of its commitment to genomic medicine, the hospital was selected as a Cancer Genomic Hub Hospital in fiscal year 2023. As part of this initiative, the hospital initiated the implementation of a comprehensive cancer panel with in-house expert panel consultations. This effort further strengthens the hospital's genomic analysis capabilities.
This presentation aims to showcase the evolutionary journey of genomic analysis at our institution, highlighting the milestones and achievements in cancer genomics. The hospital's advances in genomic medicine have not only contributed to the advancement of cancer research, but also improved patient care and outcomes.

Onsite Poster Session 15 [Others 2]
P15-4 10013

Experience of Comprehensive Cancer Genome Profiling Test in Intrahepatic Cholangiocarcinoma in Our Institution

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Background: Intrahepatic cholangiocarcinoma (ICC) is a poor-prognosis disease, and the efficacy of drugs is limited. In 2019, the comprehensive genome profiling (CGP) test was approved in Japan, and is now widely used in clinical settings. Furthermore, pemigatinib was approved in 2022 for FGFR2 fusion-positive cholangiocarcinoma in and further possibilities of CGP test are expected in the future.
Methods: Between November 2020 and April 2023, CGP test and expert panel were conducted for 11 ICC patients at our institution. Clinical data and genomic profiles were collected retrospectively, and the usefulness of CGP test was evaluated.
Results: The median age of patients was 71 years, and 6 (55%) were female. CGP test was performed on tissue-based for 6 (55%) patients and plasma-based for 5 (45%) patients. MSI-H and FGFR2 fusion gene were detected each in one case. MSI-H ICC patient achieved a complete response with pembrolizumab monotherapy. There is currently no approved drug, but actionable gene alterations, such as BRCA2 and IDH-1, were detected in 4 patients (36%). The frequency of these mutations was higher in ICC than that in other cholangiocarcinoma (11%).
Conclusions: New treatment drugs were found in some ICC patients through CGP test, and several actionable mutations were detected in ICC patients. Some clinical trials of new drugs targeting these driver genes are currently ongoing. The CGP test will provide more treatment options and improve prognosis of ICC patients in the future.

APASL Oncology 2023 Sendai

"In Search of Silver Bullet for HCC"

Abstracts

E-Posters

E-Posters [Case Report]
E-1 10001

A Case of Hepatocellular Carcinoma Associated with Glycogen Storage Disease Type Ib

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Background: The case was a 36-year-old woman. She was diagnosed as glycogen storage disease type Ib (GSD- Ib) at birth and had a history of surgery for hepatocellular adenoma at the age of 20. She was referred to our department because liver dysfunction was observed when she gave birth at the age of 30.
Results: Ultrasonography revealed a 15 mm-sized mass in S6 with hypoechoic peripheral zone and mosaic pattern of internal echoes. Dynamic CT showed 15 mm hypoattenuation area in S6. Gd-EOB MRI revealed intense enhancing tumor on arterial phase, although, the tumor showed iso-intensity on portal and delayed phase. Washout finding was not identified at hepatobiliary phase. The tumor was not identified on Diffusion -weighted image, but the tumor showed a high intensity on T2-weighted mage. It was difficult to distinguish hepatocellular adenoma (HCA) from hepatocellular carcinoma (HCC), however, contrast-enhanced US revealed hyper vascular nodule in the early vascular phase and defect in the portal and Kupffer phase. Based on these examinations, the tumor was preliminarily identified as hepatocellular carcinoma and we performed radiofrequency ablation. Pathological examination showed that the tumor was hepatocellular carcinoma.
Conclusion: GSD-I is associated with various complications including HCA and HCC. GSD-I patients manifest a metabolic phenotype of impaired glucose homeostasis and long-term risks of HCA/HCC that develops in 75% of GSD-I patients over 25 years old. The hepatic adenoma in GSD-I patients has a potential of malignant transformation, which should be keep in mind in follow-up process of the disease.

E-Posters [Case Report]
E-2 10008

A Case of Large Hepatic Hemangioma with Extrahepatic Growth and Indicated for Resection

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Introduction: Hepatic hemangiomas are the most commonly detected benign tumors, but surgical resection is indicated in large hemangiomas.
Case report information: The case was a 51-year-old man. He was referred to our hospital, because liver tumor was observed when he underwent medical check-up. Abdominal ultrasonography showed 20mm sized hyperechoic nodule, and the tumor was diagnosed as liver hemangioma. Sonographic follow up was performed and the tumor increased by 90mm with extrahepatic growth.
Treatment: Abdominal ultrasonography showed a large heterogeneous tumor with hyperechoic pattern. Dynamic contrast-enhanced CT showed a low-density, heterogeneous mass in plain phase, peripheral nodular enhancement with progressive centripetal filling in arterial phase, and prolonged enhancement during the portal and delayed phase. On Gd-EOB-DTPA-enhanced magnetic resonance imaging, the tumor showed low signal intensity on axial T1 weighted images, and high signal intensity on axial T2 weighted images. The tumor showed hyperintense signal on diffusion-weighted imaging. The tumor was compatible with hemangioma, but the patient underwent a lateral segmentectomy to avoid rupture.
Discussion: Size increase, persistent abdominal pain, superficial location of tumors larger than 5 cm with a risk of rupture. Rupture of hemangioma has a high mortality rate ranging from 60-75%, and the operative mortality rate of ruptured hemangioma was reported to be 36.4%. Therefore, large hemangioma with extrahepatic growth is considered a relative indication for surgery.
Conclusion: Large and extra growth of hemangioma may be needed strict and short-term follow-up, and operative treatment should be reserved.

E-Posters [Case Report]
E-3 10011

Primary Hepatic Methotrexate-associated Lymphoproliferative Disorders 5 Months after Methotrexate Administration

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A 71-year-old woman who had undergone a thorough examination for fever of unknown origin since November 202X was diagnosed with adult-onset Still's disease. She had diabetes mellitus and was treated with insulin injections and oral medication. The patient was administered prednisone 30 mg per day in February 25, 202X+1 and methotrexate (MTX) 6 mg per week two weeks later. Since she was a hepatitis B virus (HBV) carrier, a nucleic acid analog was also started to prevent HBV activation. CT and PET scans showed no obvious tumors in the liver or in any of the other organs. Eight weeks later, tocilizumab was started every other week. After 5 months of MTX administration, a solitary liver tumor measuring 37×32 mm was detected. Three months later, a repeat CT scan revealed that the liver tumor had grown rapidly to 7 cm. We considered the possibility of methotrexate-associated lymphoproliferative disorders (MTX-LPD) and hence stopped MTX. Biopsy specimens of the liver tumor demonstrated lymphocyte proliferation which was consistent as MTX-LPD. The doubling time for tumor growth was 33 days. In spite of the 6-week withdrawal of MTX, the tumor continued to grow, so the patient was referred to the hematology unit and treated with R-CHOP therapy. xIn the 11 previously reported cases of MTX-LPD of hepatic origin, the average duration of MTX administration was 7.3 (2-13) years. We reported here that a primary hepatic MTX-LPD-associated tumor rapidly increased in size after a very short period of MTX administration.

E-Posters [Case Report]
E-4 10019

Hepatocellular Carcinoma & Hepatic Cystic Echinococcosis Presenting as Synchronous Single Lesion

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Background: It's very rare for liver cystic echinococcosis (CE) and HCC to co-exist. Studies have shown that E. granulosus infection promotes proliferation of HCC cells by immunomodulation. A preoperative diagnosis may be very challenging, when imaging features are atypical and if HCC and CE present as a single lesion.
Case: A 35 yr old female complaining of gradual onset RUQ pain abdomen*2 months with abdominal distension and low-grade fever*2 weeks. Ascitic fluid analysis showed low SAAG, presence of free hooklet & protoscolex. TPCT abdomen s/o large heterogenous, hypoattenuating mass (12*8.5*13.5cm) in right lobe on contrast administration, peripheral rim and linear enhancements seen at multiple sites with non-enhancing large central necrotic area & tumor thrombus in Portal vein. Background liver was non-cirrhotic. Tumor markers (AFP=2.8ng/ml,PIVKA II=21mAU/ml) were within normal limits. Viral hepatitis markers were negative. Ant echinococcal Ig-G was positive. In view of diagnostic dilemma, she underwent USG guided liver biopsy; histology s/o well differentiated HCC & IHC showed HepPar-1, Arginase, Glypican-3, INSM-1 and TTF-1 positivity. She was finally diagnosed as HCC(BCLC-C) combined with hepatic hydatid disease with probable rupture into peritoneal cavity. She was administered long term oral Albendazole & TACE cycles.
Conclusion: HCC and hepatic hydatid cyst synchronous presence is very rare scenario in clinical practice, especially in a non-cirrhotic background both presented as a single lesion which poses great challenge for preoperative diagnosis. Awareness of such association will help clinicians in formulating proper management.

E-Posters [Case Report]
E-5 10021

A Case of Hepatocellular Carcinoma with Lung Metastasis that has been Controlled for more than 1 Year with Cabozantinib Introduced as the Fifth Line of Therapy

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Background: We report a case of hepatocellular carcinoma (HCC) with lung metastasis that has been controlled with cabozantinib for more than 1 year.
Case: A 60-year-old man with Hepatitis C developed HCC (S5 single, 30 mm) 12 years ago and underwent resection. Thereafter, HCC repeatedly recurred and was treated with TACE, ablation, and resection. However, HCC was poorly controlled, and lenvatinib was introduced 4 years ago. After 13 months, it became a progressive disease (PD). Sorafenib was introduced as a second line, but PD occurred after 4 months. Atezolizumab and bevacizumab were introduced as the third line; pulmonary metastases achieved partial response (PR) and intrahepatic lesions became stable. Nine months later, he developed ruptured esophageal varices. The intrahepatic lesion became PD, and TACE was performed. Lenvatinib was reintroduced as the fourth line; however, lung metastases gradually increased, and he became PD after 8 months. When cabozantinib was introduced as the fifth line treatment, the lung metastases shrank and achieved PR. Adverse effects included an increase in grade 1 ALT and AST in CTC AEs. He has been receiving cabozantinib 20 mg/day every other day for more than 1 year, effectively controlling the HCC.
Conclusion: Cabozantinib suppresses the VEGF pathway and inhibits tyrosine kinase activities, such as MET and AXL. It may have a long-term antitumor effect. Furthermore, cabozantinib can be administered at a reduced dose to maintain therapeutic efficacy while reducing adverse effects.

E-Posters [Case Report]
E-6 10048

Atezolizumab Plus Bevacizumab Enable to Perform Conversion Surgery for a Lymph Node Metastasis of Hepatocellular Carcinoma

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Aim: We report a valuable case of lymph node metastasis of hepatocellular carcinoma (HCC) in which complete response (CR) was confirmed by conversion surgery following control by atezolizumab plus bevacizumab.
Case Presentation: A 80-year-old female was followed up in our hospital for chronic hepatitis C. She had a past history of treatment for HCC. Approximately 10 years later, local recurrence was detected and treated by radio-frequency ablation. About 9 months later, a lymph node swelling (approximately 2 cm) in hepatic portal region was detected and showed strong accumulation [SUV(max) 9.6] by fluorodeoxyglucose-positron emission tomography. Taken together, we diagnosed the lesion as the lymph node metastasis of HCC. We consulted with surgeons and found that the metastasis was operable but the size and location of lymph node metastasis obliged the patient to receive pancreatoduodenectomy that was too invasive. Then, we decided to start systemic chemotherapy to perform radical operation minimally invasive. We treated the patient with 3-weekly cycles of atezolizumab/bevacizumab. The patient was well tolerated and adverse events were deterioration of hypertension and temporal increase of uric protein. Total 4 cycles of therapy were completed. Abdominal CT findings showed that CR was obtained based on Revised RECIST guideline (version 1.1). Then, lymph node dissection and cholecystectomy were performed. Subsequently, we confirmed that there was no pathological metastatic lesion in the resected lymph node.
Conclusion: Our case is the first report that we succeeded in an induction of conversion surgery to lymph node metastasis of HCC by atezolizumab/bevacizumab therapy.

E-Posters [Case Report]
E-7 10077

Chameleon Sign in CT Images of Breast Cancer Liver Metastases

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Background: We report a case of liver metastasis from breast cancer with unique CT findings.
Case: A 49-year-old woman, who became aware of a lump in her right breast and a mass in her axilla in the summer of 20XX. Suspecting breast cancer, she was referred to our hospital. ER+, PgR+, HER2 (1+). Initial treatment consisted of chemotherapy and mastectomy + axillary lymph node dissection at 20XX+1 October. ypT2N2aM0 Stage 3A postoperative chemotherapy with capecitabine. In January 20XX+2, she visited a cancer center, and in March 20XX+3, she was referred to a local doctor, who recommended endocrine therapy. In February 20XX+4, bone scintigraphy and PET-CT showed multiple liver metastases, multiple thoracic spine metastases, rib metastases, supraclavicular lymph node metastases, and multiple lung metastases, and the patient returned to our hospital in March 20XX+4. Ultrasonography revealed multiple hypoechoic masses. Non-enhanced CT depicted it as multiple low-density areas, but contrast-enhanced CT obscured the multiple masses. Tumor biopsy was performed uneventfully under ultrasound and was positive for adenocarcinoma, GATA-3, consistent with breast cancer liver metastasis.
Discussion: Contrast-enhanced CT is generally considered to have the best ability to delineate metastatic liver cancer. Some breast cancer liver metastases are oligometastatic and are low density on simple CT and slightly stained on contrast with iso density similar to that of the surrounding liver parenchyma (Radiol Oncol. 2021 19;55(4):418-425).
Conclusion: In cases of liver metastases from breast cancer, not only contrast-enhanced but also simple CT should be performed.

E-Posters [Case Report]
E-8 10078

Clinical Study of Hepatocellular Carcinoma with Bone Metastasis Treated with Palliative Radiotherapy

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Background: As recent advances in chemotherapy have increased the survival time of patients with hepatocellular carcinoma (HCC), the number of patients with extrahepatic metastases has increased. Bone metastases associated with advanced HCC are the second most common after lung metastases, causing symptoms such as pain and paralysis, significantly reducing patients' quality of life and worsening PS. Here we report on the clinical evaluation of HCC patients with bone metastases receiving palliative radiotherapy.
Methods: Five patients were diagnosed with bone metastases due to HCC and received radiotherapy from February to November 2022 in our department. Clinical parameters such as disease duration of HCC, etiology of liver disease, site of bone metastasis, and blood tests were reviewed.
Results: The mean age of the patients was 71 years, 4 males and 1 female, and the etiology of liver disease was HBV in 2, HCV in 1, and alcohol in 2 cases. The mean time from diagnosis of hepatocellular carcinoma to the onset of bone metastasis was 41 months, and the thoracic spine was the most common site of bone metastasis. All patients had previously received systemic chemotherapy. They all achieved pain relief after radiotherapy for bone metastases, and the mean prognosis after radiotherapy was 8.2 months.
Conclusions: Palliative radiation therapy was effective in relieving pain in patients with bone metastases from HCC. The mean prognosis after bone metastasis was more than 6 months, and palliative radiotherapy should be considered to maintain the PS that is needed to continue aggressive treatment for HCC.

E-Posters [Case Report]
E-9 10089

A Case of Bile Duct Stenosis after Percutaneous Ablation Therapy that was Successfully Treated with Drainage

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Background: Local ablation plays an important role in the treatment of liver cancer. Especially in HCC, the results of the SURF trial showed that local ablation was comparable to resection in terms of recurrence-free survival and overall survival. Furthermore, in Japan, local ablation, which is relatively less invasive, is often chosen due to the aging of patients and complications. On the other hand, local ablation has unique complications, and countermeasures against them are of paramount importance for safe treatment.
Case: 73 years old female with chronic hepatitis C. 2009 Peg-IFN + Ribavirin. December 2012 first S6 2.5cm single RFA. April 2015 S6 2.5cm, S6 1.0cm RFA. October 2015 SOF + LDV started and SVR. February 2016 S8, S3, S3, S6. RFA with recurrence; August 2019 RFA with recurrence; January 2020 MWA with recurrence; February 2022 hospitalized for bile duct stenosis after RFA. Hilar bile duct stenosis Bismuth IV was observed; PTCD was inserted from B2 and then the drainage area was extended to B2+B6. The patient is now under observation with sodium correction.
Discussion: Complications requiring Interventional drainage, such as the present case, correspond to Major complication: in a review of 15,744 patients (RFA 13,044 MWA 2,700), the incidence of Major complication was 4.1% for RFA and MWA 4.6% with no statistically significant difference.
Conclusion: The prognosis for complications of local ablation therapy can be improved by the concerted efforts of the gastroenterology department. Further efforts to prevent complications and avoid serious complications through early detection are necessary.

E-Posters [Case Report]
E-10 10090

Successful Response to Immune Checkpoint Inhibitor Therapy After Radiation Treatment in a Case of Stage IVb Hepatocellular Carcinoma

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Case: Patient: A 75-year-old male. Medical history: Diabetes, hypertension (under treatment at a local clinic). In March 2022, he presented with right shoulder pain and was diagnosed as having multiple hepatocellular carcinomas, as well as metastases to the right scapula and sacrum, leading to hospitalization.
Initial Examination Findings: Alb: 4.0 g/dL, Tbil: 0.9 mg/dL, AFP: 17357 ng/mL, PIVKA-II: 944 mAU/mL, HBsAg+: positive, HBVDNA: 1.6 Log/mL.
CT Findings: A large 58-mm tumor protruded into segment 2 of the liver and diffuse low-contrast tumors had spread in segment 4, with multiple 10-25-mm tumors observed in both lobes. Portal vein invasion extending to the left lobe was identified. Multiple bone metastases measuring 30 mm in the right scapula and 55 mm in the sacrum were observed.
Course: Radiation therapy (30 Gy) was administered to the right scapula and sacrum. A radiation dose of 30 Gy was also applied to the portal vein where hepatocellular carcinoma had invaded. The treatment included tenofovir disoproxil, atezolizumab, and bevacizumab. After 12months of treatment, there was sustained shrinkage of the bone metastases and hepatocellular carcinoma, maintaining a partial response (PR). [Discussion]In this case, the combination of radiation therapy to the bone metastases and portal vein invasion likely enhanced the effectiveness of atezolizumab and bevacizumab.
Conclusion: We have experienced a case of stage IVb hepatocellular carcinoma with portal vein invasion in which there was a successful response to multidisciplinary treatment. Combined use of radiation therapy may enhance the effects of immune checkpoint inhibitors, providing a potentially promising therapeutic approach.

E-Posters [Case Report]
E-11 10091

A Case of Post-RFA Hemothorax Improved with IVR and Intrathoracic Hematoma Removal

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Background: Radiofrequency ablation (RFA) for liver tumors is highly safe, and the complication of hemothorax is rare. We report a case of hemothorax after RFA. It was treated with transcatheter arterial embolization (IVR) and intrathoracic hematoma removal.
Case: A 70-year-old man with alcoholic cirrhosis had multiple HCCs of 20 mm and 15 mm in S6 and 28 mm in S8 on CT examination in March 2023. In April 2023, RFA was performed for three HCCs. We confirmed the progression of anemia with blood test after 4 hours of RFA. Right hemothorax and extravasation of the contrast medium from the right intercostal artery were found with CT examination. Hemostasis was achieved by emergency IVR, but additional intrathoracic hematoma removal was performed due to increased right hemothorax and mediastinal shift. Postoperatively, the disappearance of the right hemothorax was confirmed, and the patient was discharged.
Discussion: In this case, hemostasis was obtained by IVR, but we thought that the respiratory condition will be getting worse due to increased right hemothorax and mediastinal shift, so additional intrathoracic hematoma removal was performed. This time, we early improved hemothorax with both IVR and intrathoracic hematoma removal. Hemothorax is a post-RFA complication, and it is necessary to understand the treatment method.
Conclusion: We experienced a case of hemothorax after RFA. We will report with the consideration of the literature.

E-Posters [Case Report]
E-12 10094

A Case of Remission of Advanced Hepatocellular Carcinoma with Vascular Invasion Treated with Radiation and Sorafenib Combination Therapy

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Case: 82 years old, male [chief complaint] hepatic dysfunction [current medical history] anorexia since May 2019, he visited a local doctor who found hepatic dysfunction and also found positive HCV-RNA. Abdominal ultrasonography showed a hypoechoic mass in the right lobe of the liver, and the patient was referred to our department for further examination and treatment.
CT findings: A 70 mm large multinodular extensive mass was found in the main S6 of the liver, with a clear washout in the portal vein phase. A tumor thrombosis was formed from the right branch of the portal vein to the main trunk of the portal vein.
Outcome: After diagnosing BCLC-C advanced HCC and irradiating portal vein tumor thrombosis with 45 Gy, the patient was started on sorafenib 400 mg as systemic chemotherapy. Two months after treatment, CT showed that the HCC mainly in the right lobe of the liver had shrunk in size and become low contrast. Furthermore 6 months after treatment, the HCC and portal vein tumor thrombosis had almost disappeared, and the AFP tumor marker had normalized. The patient continues to receive sorafenib and remains in remission.
Discussion: Advanced HCC with portal vein invasion generally requires multidisciplinary treatment. Sorafenib alone is not effective for portal vein tumor thrombosis. In this case, the patient may have responded well to molecular targeted therapy after irradiation.
Conclusion: The combination of conventional irradiation and molecular-targeted therapy may enhance the therapeutic effect.

E-Posters [Case Report]
E-13 10124

The Value of Ultrasound in Diagnosing Coexisting Primary Liver Tumor and Renal Amyloidosis in a Patient with COPD: A Case Report

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Introduction: This case report describes an 83-year-old male patient with a history of COPD who presented with abdominal pain and discomfort. Ultrasound imaging was performed to assess liver lesions and signs of amyloidosis in the kidneys. Considering the patient's age, comorbidities, and COPD history, careful evaluation of potential interventions for the liver lesions is necessary.
Ultrasound findings: The ultrasound examination revealed solid liver lesions with nodular borders and a hypoechoic halo. The larger lesion, measuring 60x37 mm, was found adjacent to or invasive of the left hepatic vein, while a smaller lesion (17x15 mm) was located in segment 4. Both lesions exhibited moderate vascularity.
Diagnosis: The liver lesions were diagnosed as primary malignant tumors. Additionally, the patient exhibited diffuse kidney amyloidosis characterized by enlarged kidneys, diffusely hyperechoic renal parenchyma, poorly identified renal pyramids, and subcapsular cysts. Doppler ultrasound revealed reduced blood flow in the arcuate vessels of both kidneys, elevated resistive indices (0.81 in the right kidney and 0.83 in the left kidney), and preserved mean systolic velocity (up to 60 cm/sec) in both kidneys.
Conclusion: The presence of liver lesions and diffuse kidney amyloidosis in an elderly patient with COPD presents a complex medical situation. Further evaluation and careful consideration of potential interventions were conducted to determine the best course of treatment for the patient.

E-Posters [Case Report]
E-14 10125

Not the Usual: Diagnostic Dilemma in a Large Well Differentiated, Non- AFP Producing Hepatocellular Carcinoma with Atypical Features on Non-Invasive Imaging

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Background/Objectives: Hepatocellular Carcinoma can present with varying characteristics leading to atypical imaging findings. The classical features during imaging phases may not always be appreciated, posing diagnostic challenges. Establishing a definitive diagnosis is crucial for decision-making on management and treatment options.
Case Presentation: A 66-year-old male presenting with three months history of progressive right upper quadrant pain, easy fatigability and weight loss. Initial workups revealed elevated liver enzymes, prolonged INR, previous hepatitis B infection, and normal CEA, C19-9, AFP. Abdominal Ultrasound and CT showed cirrhosis and multiple liver masses with malignant characteristics. PET-Scan was negative for metastasis. Percutaneous liver biopsy was equivocal showing atypical malignant cells (CK7+,CK20-,HepPar-).
Discussion: Diagnostic imaging tests were conducted, including Liver Elastography (F4) to stage fibrosis in chronic liver disease and Four-phase Dynamic CT Scan to describe lesions. LI-RADS interpretation showed several arterially enhancing lesions with no washout, suggesting Atypical HCC or Combined HCC-Cholangiocarcinoma (Fig1). MRI of the Liver was also performed, showing early enhancing foci without demonstrable washout(Fig2). Both CT and MRI results were inconclusive, leading to a Laparoscopic-Guided Biopsy, revealing well-differentiated hepatocellular carcinoma (CD34+, CAM5.2+, Glypican3-)(Fig3). The patient was classified as Advanced Stage by BCLC criteria. Systemic therapy with Lenvatinib 12mg/tab once daily was initiated.
Conclusion: HCC can often be diagnosed non-invasively through CT and MRI based on distinctive imaging findings. However, when both modalities are inconclusive, biopsy becomes necessary. Understanding the complexities of hepatocarcinogenesis and the atypical features of HCC on imaging is crucial for accurate diagnosis and effective treatment planning.

E-Posters [Case Report]
E-15　10126

A Case of Hepatocellular Carcinoma Associated with Hepatic Sarcoidosis

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Background: Sarcoidosis is characterized by the formation of non-caseating granulomas throughout the body. Hepatic sarcoidosis is usually asymptomatic and is often detected due to liver dysfunction. While the majority of cases respond positively to steroid therapy and exhibit a favorable prognosis, a small proportion can progress to cirrhosis, and, in rare circumstances, hepatocellular carcinoma (HCC) may arise. In this report, we detail a case of HCC that developed in the context of hepatic sarcoidosis complicated by cirrhosis.
Case Description: A 68-year-old male presented to his primary care physician in 2016 with liver dysfunction. Laboratory tests revealed positive antinuclear antibodies and elevated IgG levels, while abdominal ultrasonography suggested cirrhosis. As a result, a liver biopsy was performed. The biopsy findings included severe hepatic fibrosis and non-caseating granuloma, leading to a diagnosis of cirrhosis in the context of hepatic sarcoidosis. He was started on steroid therapy and was closely monitored. However, in 2022, a CT scan demonstrated a 10 mm mass in S3 and a 15 mm mass in S7, both showing early dark staining and washout in the equilibrium phase, prompting referral to our department for further management. The findings on EOB-MRI were consistent with the CT scan. He underwent radiofrequency ablation for the two lesions. A follow-up CT scan one-week post-procedure revealed no apparent remnants of the lesions.
Discussion: Although most hepatic sarcoidosis cases have a good prognosis, a small percentage may progress to cirrhosis, and HCC may rarely complicate the disease. Therefore, meticulous follow-up is of utmost importance.

E-Posters [Case Report]
E-16　10138

Successful Treatment of Hepatocellular Carcinoma by Radiofrequency Ablation with Indocyanine Green Fluorescence Laparoscopy

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Background: Small hepatocellular carcinoma (HCC) located near the surface of the liver is rarely difficult to detect even by laparoscopic view and intraoperative ultrasound, which have better detectability compared to percutaneous ultrasound. In this case report, we present successful radiofrequency ablation (RFA) for a tumor that remained undetected by laparoscopic observation and ultrasound, but was made visible using Indocyanine Green (ICG) fluorescence laparoscopy.
Case: A 77-year-old female with hepatitis B viral cirrhosis was referred to our hospital for the treatment of two HCCs: one was located deep in segment 7 (<15 mm in diameter), and the other on the surface of segment 8 (<15 mm). Although both lesions were diagnosed by CT and MRI, they were hard to visualized through percutaneous ultrasound. Subsequently we conducted laparoscopic RFA after administrating ICG. While the lesion in segment 7 was visualized using laparoscopic ultrasound, identifying the lesion on the surface of segment 8 was difficult under white light laparoscopy and ultrasound. Nevertheless, ICG fluorescence observation provided clear visualization, and both lesions were effectively ablated, with following CT confirming adequate ablation effects.
Conclusion: ICG fluorescence staining enhances the visualization of the liver surfaces lesion during laparoscopic RFA for HCC when conventional imaging methods face difficulties.

E-Posters [Case Report]
E-17 10143

Imaging Insights into the Diagnosis and Management of Gallbladder Lesions in a High-Risk Patient: A Case Report

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This is a case report of an 87-year-old male with heart failure who presented with pain in the right upper abdomen. Initial ultrasound evaluation revealed chronic calculous cholecystitis with a lesion in the gallbladder, characterized by an enlarged gallbladder with walls up to 4-5 mm thick. A solid isoechoic formation with hilly contours measuring 15x20x18 mm, containing few, randomly located vessels, was detected. The ultrasound also identified sludge and hyperechoic inclusions within the gallbladder's lumen, while the intrahepatic bile ducts measured 1.5 mm. Further imaging with MRI showed an enlarged gallbladder with walls thickened up to 4-5 mm and a local thickening of up to 10 mm in the bottom area. A parietal structure measuring 17x10 mm was identified in the body area, suggestive of a neoplastic lesion. Given the patient's age and comorbidities, surgical intervention was deemed high-risk, and active observation with ultrasound monitoring was recommended to assess the potential malignancy of the gallbladder lesion. After further monitoring, the patient underwent laparoscopic cholecystectomy. The pathological examination revealed an adenocarcinoma of the gallbladder's fundus, biliary type, with a Grade 1 differentiation and a tumor size of 1.5 cm. Follow-up ultrasound performed two months after the surgery showed normal findings in the liver, bile ducts. In conclusion, this case report highlights the challenges in diagnosing and managing gallbladder lesions in high-risk patients. Imaging modalities, such as ultrasound and MRI, play crucial roles in identifying and characterizing these lesions, guiding treatment decisions, and postoperative follow-up.

E-Posters [Case Report]
E-18 10144

Case Report: Coexisting Liver-Gallbladder Oncology with Calculous Inflammation and Cholestasis - A Comprehensive Ultrasonographic Evaluation

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Introduction: We report a case of a 62-year-old female with abdominal pain during one month. Ultrasonography was conducted to investigate the underlying cause, revealing multiple abnormalities involving the gallbladder, liver, and adjacent structures.
Ultrasound Findings: The ultrasound revealed a distended gallbladder measuring 110 x 40 mm with thickened walls (6-10 mm) and containing a 38 x 30 mm calculus and sediment. The liver exhibited increased echogenicity, heterogeneity, and numerous small areas of increased echogenicity without distinct boundaries. The intrahepatic bile ducts were deformed, with individual gas bubbles, and the extrahepatic bile ducts were dilated. Additionally, a fluid mass (25 x 10 mm) adjacent to the pancreatic head contained iso- and hyperechogenic inclusions, challenging assessment of its connection with the surrounding ducts due to flatulence.
Surgical Intervention and Outcome: Surgery was recommended for further evaluation, and upon exploration, gallbladder malignancy was confirmed. The operation, however, was complicated by chronic inflammatory changes and extensive scar tissue in the region.
Discussion: This case underscores the importance of timely detection of gallbladder malignancies coexisting with calculous inflammation and cholestasis. Early identification would have likely led to a less complex surgical procedure, potentially improving the overall outcome for the patient.
Conclusion: Early detection plays a critical role in managing gallbladder malignancies presenting with calculous inflammation and cholestasis. In this case, ultrasound aided in identifying the gallbladder mass, leading to surgical confirmation of malignancy. Healthcare providers should remain vigilant in assessing such findings, enabling optimal treatment and improved patient outcomes.

なんとかしたい。
だから、挑む。

人類の歴史にはさまざまな挑戦者がいた。どんなに失敗しても、彼らの熱意や想いが何度も立ち上がらせ、その結果、常識を打ち破り新しい世界を見せてくれた。医薬はどうだ。空を自由に飛び、宇宙にまで届く時代に、私たちの体の中には未解決の課題が山積している。私たちにはやるべきことがある。助けなければならない人がいる。だから、挑む。住友ファーマは、革新的な医薬品や医療ソリューションの研究開発をより加速させる。研究重点3領域の精神神経、がん、再生・細胞医薬に加えて、感染症、糖尿病、医薬品以外のフロンティア領域で存在感を高めるために、挑み続けます。

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薬価基準収載

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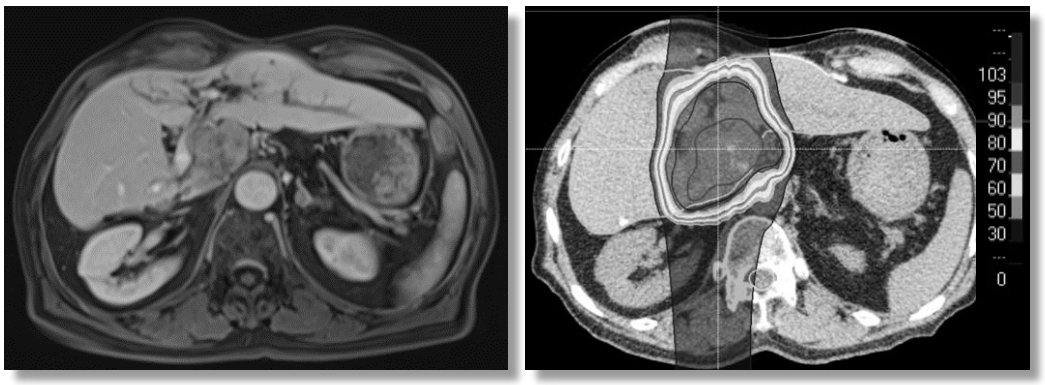

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待っている人がいる。

ギリアドは、信じています。
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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。
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