Welcome Message from the President of the APASL STC 2017, on HCV and Co-Infections

Welcome Message from the Scientific Committee Chairman

Organization

Organizing Committee
Scientific Committee
APASL Steering Committee
APASL Executive Council
Acknowledgements

General Information

Social Programs
Map and Transportation
Floor Panel

Program at a Glance
Presentation Guidelines
Scientific Programs
Luncheon Symposium

Oral Presentations
Poster Exhibitions
Welcome Message from the President of the APASL STC 2017 on HCV and Co-Infections

Professor Baatarkhuu Oidov
President
APASL - STC 2017 6th HCV Conference on HCV and Co-Infections
President Mongolian Association for the Study of Liver Disease

Dear Colleagues,

On behalf of the organizing committee of APASL STC 2017, we would like to invite you to the APASL-STC on HCV and Co-Infections will be held in on June 16-18 at Shangri-La Hotel, Ulaanbaatar, Mongolia.

Due to advances made in understanding of HCV and development of many all-oral DAAs in recent past, management strategies of HCV and coinfections are changing rapidly these days. There is growing need to share more information, provide training, and learn more about nature of HCV and co-infections both in the region and at the global level.

New research with respect to patients with mono and co-infections, disease progress, complications, basic science and current guidelines will be discussed with world opinion leaders in the field. The conference will also provide great opportunities to network decision makers, top scientists and hepatologists.

The meeting will be held in Ulaanbaatar, the modern capital of Mongolia, an ancient nomadic empire established by Huns and Chinggis Khaan. We enthusiastically invite you to submit abstracts and join us in this conference as well as our beautiful country-Mongolia.

This conference is jointly organized by Asian Pacific Association for the Study of the Liver and Mongolian Association for the Study of Liver Diseases.

We are looking forward to seeing you in Ulaanbaatar.

Sincerely yours,

Professor

Welcome Message from the Scientific Committee

As a country that suffered most by liver diseases including HCV, HBV,
Scientific Committee Chairman,
APASL STC 6th HCV Conference on HCV and Co-Infections HBV/HDV, liver cirrhosis and liver cancer, we as a nation happy to host this important meeting in the heart of Asia, beautiful city of Ulaanbaatar, Mongolia.

You are the modern day champions, heroes with a white coat, who face challenges of this once deadly disease of chronic hepatitis infection.

We are here not only to share our clinical experiences, but to sum up current progresses, discuss national programs, help each other to have a better, healthier future in our home countries and worldwide.

We especially thank the President of our country, his excellence Ts. Elbegdorj for accepting our request to organize this meeting under his patronage.

We thank the Ministry of Health for their support and actions they take against viral hepatitis. We anticipate they will incorporate our suggestions regarding national programs on viral hepatitis and liver cancer.

We have a WHO session in this meeting, during which we will be discussing current guidelines on viral hepatitis treatment and diagnosis.

It provides a great opportunity for Mongolian hepatologists, GI doctors to learn from world’s leading professionals regarding their treatment strategies and future prospective in the field.

We have Post-Graduate training for our young doctors

Sincerely yours,
The Asian Pacific Association for the Study of the Liver

Ever since its inception, in August 1978 in Singapore, APASL (Asian Pacific Association for the Study of the Liver) never looks back but stick to its goal towards advancing the science and practice of Hepatology.

Today it is one of the leading associations based on investigation and treatment of liver diseases in the world and the largest scientific body that upholds the standards and profession, research and create improved treatment methods for millions of liver patients particularly in the entire Asia Pacific Region.

APASL’s main objectives are to promote the latest scientific advancement and education of hepatology science, exchange of information and the development of consensus, encourage the practice of medicine in liver diseases and also coordinate scientific studies between various scientists and clinicians throughout the region.

We hold scientific educational symposia/conferences developed by leading hepatologists periodically. Our events feature expert speakers presenting the finest data in the most happening topics of liver diseases with high quality scientific technical presentations, followed by varied supporting program. Each of our events intended to meet the growing demands of hepatology as core medical specialty and offers participants the right platform to exchange research, discuss outcomes, and interact with colleagues, focused on liver diseases.

Our members include all medical professionals dedicated to hepatology — its research, practice and care. We cover the region from Manchuria in the North, to Australia in the South, to the Pacific Islands in the East and Iran in the West.

Our members are elected on their documented scientific publications. Mentoring, sharing of knowledge and dedication to professional growth and development are among the core values of APASL and its members.

Mongolian Association for the Study of Liver Disease
The Mongolian Association for the Study of Liver Disease (MASLD) started as a small group of 15 hepatologists from central and private hospitals who came together to share best medical practice in April 2009. Last 7 years MASLD has grown bigger and has over 200 members.

MASLD is an official branch of APASL and a non-profit organization that performs its duty under a written constitution. The Association is managed by the MASLD Governing Board made up of 5 elected members.

- To promote the research of the study of liver disease
- Provides state-of-the-art education for physicians and scientists
- Fosters public awareness of liver diseases and their management
- Supports young investigators to ensure that the liver remains at the forefront of research

Present president of MASLD: Professor Baatarkhuu Oidov.
Scientific committee chairman: Professor Amarsanaa Jazag

Baatarkhuu Oidov /MASLD/
Amarsanaa Jazag /MASLD/
Gerelchimeg Tsagaantsooj /MASLD/
Munkhbat Batmunkh /MNUMS/
Tumurbat Byamba /Ombol LLC/
Naranzul Nyamsuren /MNUMS/
Bulgan Baasanbyamba /Sysmex/ Corporation
Sergelen Sukhbaatar /Proliance LLC/
Tunsag Murdorj/ NCCD/
Saruul Bat-Ulzii /NCCD/
Bayarmaa Ochirkhuree /State First Hospital/
Gegebadrakh Baljinnyam /State Second Hospital/
Badamsuren Dorjgotov /State Third Hospital/
Munkh-Erdene Nanjid /Happy Veritas Clinic and Laboratory/

## Scientific Committee

<table>
<thead>
<tr>
<th>Scientific Committee Chairman</th>
<th>Name</th>
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<tbody>
<tr>
<td>Scientific Committee Chairman</td>
<td>Amarsanaa Jazag</td>
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<td>I</td>
<td>Sheikh Mohammad Fazle Akbar</td>
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<td>Sharma Barjesh Chander</td>
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<td>Chia-Yen Dai</td>
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<td>Hasmik Ghazinyan</td>
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<td>Kwang-Hyub Han</td>
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<td>Masatoshi Kudo</td>
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<td>Diana Payawal</td>
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<td>Gamal Shiha</td>
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<td>Yasuhito Tanaka</td>
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## APASL Single Topic Conference 2017

**6th HCV conference**

Ulaanbaatar • Mongolia

**16-18 June**

Tawesak Tanwandee

Lai Wei

Khin Maung Win

Osamu Yokosuka

Kim Do Young

Ming Lung Yu

Man-Fung Yuen

Cihan Yurdaydin

*Listed alphabetically by last name*

<table>
<thead>
<tr>
<th>Position</th>
<th>Name</th>
<th>City</th>
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<tr>
<td>Chairman</td>
<td>Shiv Kumar Sarin</td>
<td>New Delhi</td>
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<tr>
<td>President</td>
<td>Barjesh Chander Sharma</td>
<td>New Delhi</td>
</tr>
<tr>
<td>Immediate Past President</td>
<td>Jinlin Hou</td>
<td>Guangzhou</td>
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<tr>
<td>President Elect</td>
<td>Diana Payawal</td>
<td>Manila</td>
</tr>
<tr>
<td>Secretary General-cum-Treasurer</td>
<td>Lai Wei</td>
<td>Beijing</td>
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<td>Past Presidents</td>
<td>Darrell Crawford</td>
<td>Brisbane</td>
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<td></td>
<td>A. Kadir Dokmeci</td>
<td>Ankara</td>
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<td>Ji-Dong Jia</td>
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<td>Jia-Horng Kao</td>
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<td>George Lau</td>
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<td>Laurentius A. Lesmana</td>
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<td>Masao Omata</td>
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<td>Teerha Piratvisuth</td>
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<td>Jose Sollano</td>
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<td>Dong Jin Suh</td>
<td>Seoul</td>
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<td>Osamu Yokosuka</td>
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<td>Shahab Abid</td>
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<td>Deepak N. Amarapurkar</td>
<td>Mumbai</td>
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<td>Ian Homer Y.Cua</td>
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<td>Hasmik Ghazinyan</td>
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<td>Han-Chieh Lin</td>
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<td>Rosmawati Mohamed</td>
<td>Kuala Lumpur</td>
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<td>David Handojo Muljono</td>
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<td>Tawesak Tanwandee</td>
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<td>Alexander Thompson</td>
<td>Melbourne</td>
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<td>Fu-Sheng Wang</td>
<td>Beijing</td>
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The Organizing Committee of the APASL STC 6th HCV Conference on HCV and Co-Infections would like to acknowledge and express our sincere gratitude for the following organizations and companies for their great support.

GILEAD

SilverSponsor

SYSMEX
Mongolian Association for the Study of Liver Disease

Symposium
Date: June 16 (Friday) – June 18 (Sunday), 2017
Venue: Shangri-La Hotel
Address: 19 Olympic Street, Sukhbaatar District 1, Ulaanbaatar 14241, Mongolia

Venue: Shangri-La Hotel, 1st floor

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
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<tbody>
<tr>
<td>June 16 (Friday)</td>
<td>07:00 - 18:00</td>
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<tr>
<td>June 17 (Saturday)</td>
<td>07:30 – 18:00</td>
</tr>
<tr>
<td>June 18 (Sunday)</td>
<td>07:30 – 12:00</td>
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The official language of APASL STC on HCV and Co-Infections 2017, Ulaanbaatar is English. We regret that simultaneous translation will not be available.

www.apasl-stc2017mongolia.mn
All delegates are required to wear their official name badges at all times in Conference venues.

Accompanying persons must also wear their badges during all official programs that they attend.

**Lunch**
Lunch platter service will be placed on the table during Luncheon Symposium by showing your lunch coupon.

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Venue</th>
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<tbody>
<tr>
<td>June 16 (Friday)</td>
<td>10:55 – 11:10</td>
<td>Conference Hall</td>
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<td>16:45 – 17:00</td>
<td>Conference Hall</td>
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<tr>
<td>June 17 (Saturday)</td>
<td>11:15 – 11:30</td>
<td>Conference Hall</td>
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<td>16:20 – 16:35</td>
<td>Conference Hall</td>
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<tr>
<td>June 18 (Sunday)</td>
<td>10:15 – 10:30</td>
<td>Conference Hall</td>
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Free WiFi will be provided at the Conference Venue.

**Faculty Dinner**
- **Date:** June 16, 2017 (Friday)
- **Time:** 18:30 – 21:30 (Dinner)
- **Venue:** Broadway Restaurant
- **Dress code:** Smart casual
- **Invitation only:** Faculty dinner is exclusive to invited faculty
- **Shuttle bus service during the conference venue and dining venue is provided.**

**Gala Dinner**
- **Date:** June 17, 2017 (Saturday)
- **Time:** 19:00 – 22:00
- **Venue:** Ulaanbaatar Hotel
- **Dress code:** Smart casual
- **Invitation only:** No admittance without Gala Dinner Voucher

**Hotel Map**
6th HCV conference
Ulaanbaatar • Mongolia

16-18 June • Ulaanbaatar • Mongolia
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>07:00-08:00</td>
<td>Registration</td>
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<tr>
<td>08:00-09:30</td>
<td>Official Symposium I</td>
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<tr>
<td></td>
<td>Real-World Experiences of HCV Treatment and National Program of Viral</td>
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<tr>
<td></td>
<td>Hepatitis in Asia-Pacific Region I</td>
</tr>
<tr>
<td>09:30-10:30</td>
<td>Opening ceremony</td>
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<tr>
<td>10:30-10:55</td>
<td>Presidential lecture</td>
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<tr>
<td>10:55-11:10</td>
<td>Coffee break</td>
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<tr>
<td>11:10-12:30</td>
<td>Official Symposium II</td>
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<tr>
<td></td>
<td>Real-World Experiences of HCV Treatment and National Program of Viral</td>
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<tr>
<td></td>
<td>Hepatitis in Asia-Pacific Region II</td>
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<tr>
<td>12:30-13:00</td>
<td>Keynote lecture I</td>
</tr>
<tr>
<td></td>
<td>Management of HCV patients while waiting for DAA Approval</td>
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<tr>
<td>13:00-14:00</td>
<td>Luncheon symposium supported by Ombol LLC</td>
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<td>Management of HCC, where we are now</td>
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<td>14:00-15:50</td>
<td>Keynote lecture II</td>
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<td>Systemic therapy for Hepatocellular Carcinoma: Current Status and</td>
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<td>Future Perspective</td>
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<td>Decompensation of cirrhosis: Why and How?</td>
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<td>15:50-16:45</td>
<td>Official Symposium III</td>
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<td>Treatment strategy of HCV infection in Asia</td>
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<tr>
<td>16:45-17:00</td>
<td>Coffee break</td>
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<tr>
<td>17:00-18:00</td>
<td>Official Symposium IV</td>
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<td>Treatment strategy of co-infection</td>
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<tr>
<td>19:00-21:00</td>
<td>Faculty Dinner</td>
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<tr>
<td>Time</td>
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<tr>
<td>08:00</td>
<td>Oral presentation</td>
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</table>
| 09:00  | Keynote lecture III  
Beyond and Cure of HCV  
Liver transplantation for HCV in the DAA era |
| 09:00  | APASL-WHO Joint Session                                             |
| 09:30  | Coffee Break                                                        |
| 10:00  | Official Symposium V  
Hepatitis B virus infection                                             |
| 11:15  | Luncheon symposium supported by Sysmex Corporation                  |
| 11:30  | Official Symposium VI  
New DAA treatment and liver cirrhosis                                   |
| 13:00  | Coffee Break                                                        |
| 13:00  | Keynote lecture IV  
Acute and Chronic Liver Failure  
Evidence Based Immune Therapy for chronic hepatitis B: Proof of concept for  
management of wide-varieties of chronic liver diseases |
| 17:35  | Official Symposium VII  
Novel therapy of HCC                                                    |
| 19:00  | Gala Dinner                                                          |

**07 1906**

<table>
<thead>
<tr>
<th>Time</th>
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<tbody>
<tr>
<td>09:00</td>
<td>Post graduate course I for Mongolian doctors</td>
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<tr>
<td>09:30</td>
<td>Coffee Break</td>
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<tr>
<td>09:30</td>
<td>Post graduate course II for Mongolian doctors</td>
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<tr>
<td>01:00</td>
<td>Closing remarks</td>
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</table>

Presentation Slides
- At least 5 hours before the presentation, speakers are required to upload and preview their lecture files in the Slide Preview Room – (1st floor, Shangri La Hotel). Speakers at morning sessions are advised to do so the previous day.
• Speakers must use the equipment provided; use of personal electronic devices to make presentations is not permitted.

Stand-by
Please stand by at the session venue 20 minutes before your presentation. Start your presentation when the moderator introduces you.

Time Allocation (Presentation & Discussion):

• Postgraduate Course Lecture: 20 minutes
• Keynote Lecture: 25 minutes
• Country experiences Workshop (Official symposium I, II): 10 minutes
• APASL-WHO Joint Session: 15 minutes
• Official symposium III, VI: 20 minutes
• Official symposium IV, V, VII: 15 minutes

• 08:00–09:00 on June 17, 2017 (Saturday).
• Oral presenters will have 7 minutes for their presentation and 2 minutes for discussion.
• Presenters are required to upload and preview their lecture files in the Slide Preview Room at 13:00 on June 15, 2017.
• Presenters must use the equipment provided; use of personal electronic devices to make presentations is not permitted.
• Time control will be strictly implemented using a final countdown reminder.

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<tr>
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<td>June 17, 2017</td>
<td>08:00-19:15</td>
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<tr>
<td>June 18, 2017</td>
<td>09:00-13:00</td>
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Poster Presentations
Presenters must design and print their own posters.
Posters must be portrait format only, limited to an entire size of 90 cm wide x 150 cm high.
Authors must bring their printed posters to the Conference. Do not mail your poster to the Conference Secretariat or to the meeting site.
Materials for mounting posters will be provided in the poster area.
### Day 1

**Real-World Experiences of HCV Treatment and National Program of Viral Hepatitis in Asia-Pacific Region I**

<table>
<thead>
<tr>
<th>OS</th>
<th>Title</th>
<th>Speakers</th>
<th>City</th>
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<tbody>
<tr>
<td>OS1-1</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Armenia</td>
<td>Hasmik Ghazinyan, Jazag Amarsanaa, Barjesh Chander Sharma, Diana Payawal</td>
<td>Erevan</td>
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<tr>
<td>OS1-2</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Myanmar</td>
<td>Khin Maung Win</td>
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<td>OS1-3</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in China</td>
<td>Lai Wei</td>
<td>Beijing</td>
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<td>OS1-4</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Mongolia</td>
<td>Jazag Amarsanaa</td>
<td>Ulaanbaatar</td>
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<td>OS1-5</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Turkey</td>
<td>Cihan Yurdaydin</td>
<td>Ankara</td>
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<td>OS1-6</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in India</td>
<td>Barjesh Chander Sharma</td>
<td>New Delhi</td>
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<td>OS1-7</td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Pakistan</td>
<td>Saeed Sadiq Hamid</td>
<td>Karachi</td>
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<td>98 09′98 19</td>
<td>OS1-8 Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Russian Federation</td>
<td>Malov Igor Vladimirovich, Irkutsk</td>
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<td>98 19′98 19</td>
<td>Discussion</td>
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<td>Opening ceremony</td>
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<td>Welcome Speech by President of the APASL STC 2017, 6th HCV Conference</td>
<td>Professor Oidov Baatarkhuu</td>
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<tr>
<td>98 44′09 94</td>
<td>Welcome Speech by TBD</td>
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<td>09 94′09 09</td>
<td>Welcome Speech by Minister of Health Dr. Ayush Tsogtssetseg</td>
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<tr>
<td>09 09′09 04</td>
<td>Welcome Speech by Coordinator, HIV,STI, viral hepatitis unit, WHO WPRO Dr. Ying-Ru Lo</td>
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<td>09 04′09 19</td>
<td>Welcome Speech by Chairman of the Scientific Committee of the APASL STC 2017, 6th HCV Conference</td>
<td>Professor Jazag Amarsanaa</td>
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<td>09 19′09 19</td>
<td>VIP’s Group photo</td>
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<tr>
<td>09 19′09 44</td>
<td>HCV and Co-Infections in Mongolia Professor Oidov Baatarkhuu</td>
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<td>09 44′00 09</td>
<td>Coffee break</td>
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<tr>
<td>00 09′01 19</td>
<td>Real-World Experiences of HCV Treatment and National Program of Viral Hepatitis in Asia-Pacific Region II</td>
<td>Oidov Baatarkhuu, Saeed Sadiq Hamid, Lai Wei</td>
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<td>00 09′00 19</td>
<td>OS2-1 Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Philippine</td>
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<td>Usefulness of adjustable RFA electrode needle for liver cancer – compared to cool-tip electrode</td>
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**Discussion**

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<td>LUNCHEON SYMPOSIUM I</td>
<td>Management of HCV patients while waiting for DAA Approval</td>
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**Keynote Lecture I**

**Lunch Symposium I**

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<td>Clinical significance of Resistance-Associated Variants of HCV</td>
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<td>Treatment strategy of HCV infection in Asia</td>
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<td>Prioritization of HCV patients for alloral DAA therapy in Asia</td>
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<td>Use of DAAs in Asia with Special Reference to Generics</td>
<td>Saeed Hamid</td>
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### 06 1906 Day II

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<td>Cihan Yurdaydin, Mamun Al Mahtab, Dorjgotov Badamsuren</td>
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<td>Treatment strategy of HBV/HCV coinfection</td>
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<td>Impact of HCV therapy on preventing disease progression</td>
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<td>Treatment Strategy of HCV/HIV coinfection</td>
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**6th HCV conference**

**1906 16-18 June • Ulaanbaatar • Mongolia**

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<td><strong>06 04</strong></td>
<td><strong>08 00</strong></td>
<td>Serum vitamin D level and Bsm1 A&gt;G (rs1544410) polymorphism of VDR gene in patients with chronic hepatitis C infection</td>
<td>B. Enkh-Amar</td>
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<td>Functional and morphological abnormality of liver among diabetic patients with viral hepatitis/ M2BP GI and elastography changes comparative results</td>
<td>I. Altantuya</td>
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<td><strong>97 99</strong></td>
<td><strong>06 08</strong></td>
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<td>HCV and HBV among general population in Mongolia: Current situation based on a nationwide survey</td>
<td>D. Davaalkham</td>
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<td><strong>97 10</strong></td>
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<td><strong>08 21</strong></td>
<td>Sofosbuvir and Ledipasvir in attainment of SVR12 in sickle cell disease (SCD) sub-population with chronic hepatitis C (CHC). a single center prospective open label clinical pilot study - SLASH C Trial</td>
<td>Patrick Basu</td>
<td>Weil Cornell University Hospital</td>
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<td>Alpha-Fetoprotein response after selective internal radiation therapy versus Sorafenib in locally advanced HCC</td>
<td>Kh. Ariunaa</td>
<td>NCC</td>
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<td><strong>97 14</strong></td>
<td><strong>06 07</strong></td>
<td><strong>09 00</strong></td>
<td>Real-world experiences of HCV treatment, and brief outlook at national program of HCV eradication in Bangladesh</td>
<td>Mamun Al Mahtab</td>
<td>Bangabandhu Sheikh Mujib Medical University</td>
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<td>KEYNOTE LECTURE III</td>
<td>Diana Payawal, Khuyag Bayanmunkh</td>
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<td>Beyond and Cure of HCV</td>
<td>Masao Omata</td>
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<td>Liver transplantation for HCV in the DAA era</td>
<td>Ray Kim</td>
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<td>Masao Omata, Jazag Amarsanaa, Ying-Ru Lo</td>
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<td>Progress on hepatitis elimination</td>
<td>Ying-Ru Lo</td>
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<td>APASL HCV Treatment Guidelines</td>
<td>Masao Omata</td>
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<td>10:00</td>
<td>Paediatric HCV and mother to child transmission: overview</td>
<td>Po-Lin Chan</td>
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<td>APASL HBV Treatment Guideline</td>
<td>Diana Payawal</td>
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<td>Hepatitis B virus infection</td>
<td>Ray Kim, Pagbajab Nymadawa, Osamu Yokosuka</td>
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<td>Clinical application of HBV markers</td>
<td>Man-Fung Yuen</td>
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<td>Treatment of hepatitis B in Asia Pacific</td>
<td>Osamu Yokosuka</td>
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<td>Clinical significance of occult HBV infection</td>
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<td>TLL1 genetic variants associated with development of hepatocellular carcinoma</td>
<td>Yasuhiro Tanaka</td>
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<td>Hisashi Narimatsu</td>
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<td>Detection of new biomarker-M2BPGi level among healthy and HCV infected population: A nationwide survey</td>
<td>Davaalkham Dambadarjaa</td>
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<td>HBV and HCV infections in different social groups in Ulaanbaatar, Mongolia</td>
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<td>OS6-1 Disease staging and prognosis</td>
<td>Ray Kim</td>
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<td>OS6-2 Emerging trend in the Management of Liver Cirrhosis</td>
<td>Kwang-Hyub Han</td>
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<td>OS6-3 Treating HCV with new DAAs: Perspective from Canada</td>
<td>Samuel Lee</td>
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<td>OS6-4 Management of Hepatic Encephalophaty</td>
<td>Barjesh Chander Sharma</td>
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<td>OS6-5 Clinical Evaluation of real-world interferonfree regimens and Assessment of developing hepatocellular carcinoma after eradication of hepatitis C virus</td>
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<td>Evidence Based Immune Therapy for chronic hepatitis B: Proof of concept for management of wide-varieties of chronic liver diseases</td>
<td>Sheikh Mohammad Fazle Akbar</td>
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**Novel therapy of HCC**
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<td>Recent progress in radiotherapy</td>
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<td>New emerging transarterial therapies for unresectable HCC</td>
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Jigjidsuren Chinburen, Jinsil Seong, Manaljav Shagdarsuren
## 6th HCV conference

**07 1906**

Day III

### POST GRADUATE COURSE I

#### FOR MONGOLIAN DOCTORS

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<td>Experience of all DAAs therapy in Myanmar patients with chronic HCV infection</td>
<td>Khin Maung Win</td>
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<td>Innovative therapy in liver diseases- from bench to bedside</td>
<td>Mamun Al Mahtab</td>
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<td>National Viral Hepatitis program of Mongolia</td>
<td>N. Tungalag</td>
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<td>HBV infection: Prevalence, Diagnosis, Treatment in Mongolia</td>
<td>Ya. Dahgwhadorj</td>
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<td>Prevalence, clinical features, diagnosis, treatment and prevention of HCV in Mongolia</td>
<td>B. Saruul</td>
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<td>Prevalence, clinical features, diagnosis, treatment and prevention of HDV in Mongolia</td>
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<td>D. Badamsuren</td>
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<td>HCV treatment after curative liver resection or RFA in HCC patients</td>
<td>J. Chinburen</td>
<td>National Cancer Center</td>
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<td>Closing remarks</td>
<td>O. Baatarkhuu</td>
<td>President of the APASL STC 2017</td>
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Professor

Education and Career Background:

1991-1996 M.D. Otoch-Manramba Medical Institute (Manba-Datsan), Mongolia
1996-1997 M.S. Candidate (Transferred before graduation) National School of Medicine, Mongolia
1998-2000 Clinical Research Fellow, Department of Gastroenterology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan
2000-2002 Master degree of Science (Master of Medical Science), Graduate School of Medicine, University of Tokyo, Tokyo, Japan
Thesis: Role of Chemokine Receptors in Gastrointestinal cancers
Advisor: Masao Omata, M.D.
2002-2006 Ph.D. in Medicine, Major: Gastroenterology. Minor: Molecular Oncology of GI tract. Department of Gastroenterology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan
Advisor: Masao Omata, M.D.
2006-2008 Post-Doctoral fellow, Department of Surgery, Harvard Medical School, Brigham and Women’s Hospital Boston MA, USA

Scientific Committee Chairman

Graduated in Medicine and Surgery (MBBS) in 1980 from Bangladesh and received PhD in Medical Sciences from Ehime University Graduate School of Medicine, Ehime Japan in 1993. Worked at International Center for Diarrheal Diseases and Research from 1984-1985 and organized Diarrheal disease control program of Bangladesh until 1987 when received MONBUSHO scholarship to study in Japan. After obtaining PhD in Medicine, worked as full faculty member of Department of Gastroenterology and Metabology, Ehime University, Ehime, Japan from 1996 until 2008. Then joined as Principal Investigator at Toshiba General Hospital, Tokyo, Japan and continuing at that position till now.

Professor

The major clinical interests lie in elucidation epidemiology, pathogenesis and prognosis of chronic liver diseases and cancers. Focused on the role of antigen-presenting dendritic cells in the pathogenesis of almost all types of chronic liver diseases and various cancer. The research interest led to development of immune therapy for chronic liver diseases and cancers. Used antigen-based vaccine therapy in animal model of HBV and HCV infection and also in liver and other GI cancers. Conducted clinical trials with various novel approaches in chronic liver diseases by manipulating nature of antigens, dose of antigens, duration of therapy and route of administration of therapeutic vaccination.
Professor Oidov Baatarkhuu graduated from the Mongolian National Medical University and obtained his degree in Doctor of Medicine with commendation in 1994. He has received his PhD degree at the Postgraduate School, Health Sciences University of Mongolia in 2006. He is currently Professor of Medicine, Head of Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences and General Expert on Infectious Diseases of Ministry of Health, Mongolia.

He has completed his postdoctoral Fellowship in Hepatology at the Department of Internal Medicine, Severance Hospital, Yonsei University College Professor of Medicine, Seoul, Korea between 2007-2008. He did second overseas Clinical Research Fellowship in Hepatology at the Department of Internal Medicine III, AKH Hospital, University of Vienna, Austria in 2012. Also currently he has Department of completed as a Clinical Research Fellow in Hepatology at the Storr Liver unit, Infectious Diseases, Mongolian National University of Medical Sciences Westmead Millennium Institute for Medical Research, University of Sydney, Australia. He has also been a Visiting Professor at the Victorian Infectious Diseases Laboratory, Melbourne, Australia in 2014.

Professor O.Baatarkhuu is an Executive Council Member of APASL, Member of CEVHAP, and President of the Mongolian Association for the Study of the Liver Diseases, Executive Director of the Mongolian Infectious Diseases Physicians, Mongolia and Chairman of the Scientific Committee for the APASL-STC 2012 in Mongolia. Currently he is President of APASL-STC on HCV and Confections 2017 in Mongolia.

Professor O.Baatarkhuu is a key investigator in more than 20 international and national trials on antiviral treatment of chronic hepatitis B and C.

He has been extensively involved in research in the fields of viral hepatitis and hepatocellular carcinoma and he is currently working on the natural history of hepatitis B and D in Mongolia.

Professor O.Baatarkhuu has published more than 120 international and local papers. He has also spoken nationally and internationally on viral hepatitis and chronic liver diseases including hepatocellular carcinoma.

Professor, Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

- Hepatic Encephalopathy
- Portal Hypertension
- Cholangitis

Professor
Dr Po-Lin Chan is the Medical Officer for Viral Hepatitis, World Health Organization Western Pacific Regional Office. Po-Lin is a medical doctor trained in obstetrics and gynaecology, tropical medicine as well as epidemiology. She has worked across a variety of health settings spanning Africa, South Asia and East Asia working with communities in difficult situations to advising on health programmes. Po-Lin was Team Leader HIV/STI in WHO India where she was instrumental in the establishment, scale-up and decentralisation of the Indian national programme for HIV and STI. Until recently, she was the Senior Advisor for Viral Hepatitis/HIV and STI at WHO in China where she drives the vision on triple elimination of mother to child transmission in particular, the third-e towards zero new paediatric hepatitis infections, and on implementation of the interlinked global health sector strategies on HIV, STI, and Viral Hepatitis.

Education and Career Background:

1-30 Apr 2008 Observational training on pancreatic surgery, Salzburg, Austria
1-28 Feb 2009 Intensive training and research program in the field of HPB surgery, Aichi Cancer Center, Nagoya, Japan
1-31 July 2011 Medical scientist fellowship training on liver transplant, Samsung Medical Center, Seoul, Korea
1-28 October 2013 Observational training of HPBS, Toronomon Hospital, Tokyo, Japan

Professor

Director of National Cancer Center, President of MHPB society
Faculty:
- Assistant Professor, School of Medicine, College of Medicine, Kaohsiung Medical University,
- Associate Professor, School of Medicine, College of Medicine, Kaohsiung Medical University,
- Professor, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung Taiwan,
- Chief, Department of Occupational and Environmental Medicine, Kaohsiung Medical University Hospital,
- Chief, Department of Preventive Medicine, Kaohsiung Medical University Hospital,
- Attending Physician, Division of Hepatology, Department of Medicine, Kaohsiung Medical University Hospital,
- Vice Secretary General, Gastroenterology Society of Taiwan (GEST)

- Epidemiology of hepatitis B and C virus infection in Taiwan
- Treatment of hepatitis B and C
- Extrahepatic manifestation of chronic hepatitis C
- Genetic study
- Nature course, treatment and molecular biology of HCC
- Contrast echo image
- Occupational and environmental medicine

Professor Yagaanbuyant
Mongolian Society of Hepatology;
Mongolian Society of Biostatistics
School of Public Health, Mongolian National University of Medical Sciences

Davaalkham Dambadarjaa
1969-1975 Bachelor Degree, State Medical Institute of Mongolia
1983-1987 Ph.D Course of Medical Science Medical Institute of Mongolia
1969-1975 Bachelor Degree, State Medical Institute of Mongolia
1975-1980 chairman of Chandmanasomon’s (county) medical centre, Gobi-Altai aimak;
1980-1983 chairman of pediatric department, Unit hospital, Gobi-Altai aimak;
1987-1988 consultant doctor of pediatric and infectious diseases department, Unit hospital, Gobi-Altai aimak;
1988-1995 associate professor of the department of infectious diseases of Mongolian State Medical Institute;
1995 chairman of dept. Infectious diseases of Mongolian National Medical University and Health Sciences University

2012 Prof. of dept. Infectious diseases of Mongolian National Medical University and Health Sciences University

GCN
2003-2007 PhD in Medicine, Department of Public Health, Jichi Medical University, Japan
2007-2009 Master in Administration, Mongolian Management Academy, Mongolia

46. Davaalkham D, Ojima T, Wiersma S, Lkhagvasuren Ts, Nymadawa P, Uehara R, Watanabe M, Oki I, Takahashi M, Okamoto H, Nakamura Y. Administration of hepatitis B vaccine in winter as a significant predictor of

1994-2001 National Medical University of Mongolia (renamed into Health Sciences University), Diploma of Bachelor's Degree in Medicine

2017 Associated professor
2010 Internal medicine retraining, National Taiwan University
2006-2009 PhD degree, Health Science University of Mongolia
1999 Ultrasound diagnosis, Medical University of Mongolia
1996-1998 Master degree, Medical University of Mongolia
1996-1998 Gastroenterology and hepatology fellowship, Medical University of Mongolia

1996 Internal medicine residency, Medical University of Mongolia

Professor

Experience
From May 2015 Head of Gastroenterology department at 3th hospital named by Shastin

Department of Gastroenterology, 3rd Central Hospital

2014-2015 Gastroenterologist, hepatologist at 3th hospital named by Shastin
2012-2014 Director of training and scientific at Bayanzurkh hospital
2010-2012 Quality manager at 3th hospital named by Shastin
1992-2010 Gastroenterologist, hepatologist at 3th hospital named by Shastin
Yerevan State Medical University -1972-1978, Lecturing desk as a physician infectionist, Certificate program as Chair of infections Disease in NIH, Fellowship on infections Disease in Albany Medical Centre, NY, USA 1996- June-September Head of Hepatology Departament-1986-Present President of Armenian Hepatological Forum since 30 July 2007 Member of EASL, APASL, CEVHAP Full member (Academician) of European Academy of Natural Sciences Awarded with the medal of Rudolf Virchow for special merits, given by European Academy of Natural Sciences Main Hepatologist

Professor

Hasmik Ghazinyan

Head of Hepatological
Department, Nork
Clinical Hospital of
Infectious Diseases,
Chief Specialist of
Ministry of Health,
Yerevan, Armenia

of the Republic of Armenia Member of APASL executive Council (EC) 2017

- Viral Hepatitis (B,C,D)
- Acute on Chronic Liver Failure (ACLF)
- Alcoholic Liver Diseases
- Liver and Pregnancy
- Toxic Hepatitis
- HCC

Dr Saeed Sadiq Hamid is The IbneSina Professor of Medicine and Chairman, Department of Medicine at The Aga Khan University, Karachi, Pakistan. He graduated from King Edward Medical College, Lahore in 1981, and has been affiliated with AKU since 1990. He completed his postgraduate training in Medicine and
Professor Saeed Sadiq Hamid
Aga Khan University, Karachi, Pakistan

His research interests include Viral Hepatitis and Acute Liver Failure. He has been the recipient of basic and clinical research grants, including clinical trials. He has a total of 145 peer reviewed publications and three book chapters to his credit, and currently serves as an associate editor for Hepatology International, the official journal of APASL. Dr Hamid has been a Member of the Executive Council, Asian Pacific Association for the Study of the Liver, 2006-2010, and President, Pakistan Society for the Study of Liver Diseases from 2011-2016. He has been a long serving member of the WGO Guidelines and Publications committee and also a member of many guideline development groups of the APASL. He chaired the WHO Guidelines Development Group on HCV treatment guidelines, which were released in April 2016.

Professor Kwang-Hyub Han

1973 - 1979 GraudateYonsei University College of Medicine, Seoul, Korea
1986- present Full time faculty of Department of Internal Medicine, Yonsei University College of Medicine
2012 - Present Member of The Korean Academy of Science Technology
2013 – 2017. 2 Professor and Chairman, Department of Internal Medicine, Yonsei University College of Medicine
2015 - Present Director, Yonsei Liver Center, Severance Hospital
2016 - Hosting chairman, APASL STC 2016 in Busan
South Korea

Professor
W. Ray Kim
Stanford University
School of Medicine, San Francisco, USA

W. Ray Kim, MD, is Professor and Chief in the Division of Gastroenterology and Hepatology at Stanford University School of Medicine. Prior to assuming this post in November 2013, Dr. Kim was Professor of Medicine at Mayo Clinic College of Medicine. Dr. Kim earned his medical diploma at Seoul National University in Korea. He underwent training in gastroenterology and hepatology at Mayo Clinic in Rochester, MN. He also holds a Master in Science Degree in patient oriented research from Seoul National University and a Master in Business Administration from University of Pennsylvania. He has served on the Governing Board of the American Association for the Study ofLiver Disease (AASLD), where he currently chairs the Global Outreach and Engagement Committee.

Dr. Kim’s research interest has been in epidemiology and outcomes studies in chronic liver disease and liver cancer. His research has been funded by several NIH grants, one of which is credited for the seminal achievement of developing the Model for End Stage Liver Disease or the MELD score. With regard to research in hepatitis B, he led the multicenter team in Minnesota and served on the Steering Committee in the Hepatitis B Research Network, a Collaborative Grant by NIDDK.

1976-1986: High school №24, Ulan-Bator, Mongolia
1986-1993: Medical university of Mongolia, Ulan-Bator, Mongolia
1995-1998: University of Lausanne, Faculty of Medicine, Lausanne, Switzerland
2001- 2003: Doctor of Medicine by the thesis of "Hepatic alveolar Echinococcosis, about 21 cases" University of Lausanne, Faculty of Medicine, Lausanne, Switzerland, under supervision of Prof. M. Gillet

Professor
Khuyag Bayanmunkh

General surgeon, Liver and pancreatic surgeon,
Santso surgery clinic

• Kyoto University Faculty of Medicine (Year graduated: 1978)
• 1979-1987 Kobe City Medical Center General Hospital.
Gastroenterology
• 1987-1989 University of California
Education and Career Background:

- 1989-1997 Kobe City Medical Center General Hospital. Gastroenterology
- 1997-1999 Kindai University Hospital, Second Department of Internal Medicine
- 1999-Present Kindai University Hospital, Department of Gastroenterology and Hepatology

Professor

Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan

Clinical and Research Interest:

Diagnosis and Treatment of HCC
Treatment of Viral hepatitis (HBV, HCV)
Dr Ying-Ru Lo is an infectious disease physician from Hamburg, Germany who took up her duties at WHO in 1998. With over three decades of working experience as a clinician and public health adviser in prevention, care and treatment of HIV, viral hepatitis and sexually transmitted infections (STI) Dr Lo has worked in Europe, Latin America, Asia and the Pacific. Dr Lo is a senior staff member of the World Health Organization (WHO) with particular interest in translating research to program implementation. She has worked at three levels of the Organization (country, regional and headquarters). Dr Lo led the introduction of HIV treatment during the early nineties in South-East Asia, reinvigorated WHO’s global HIV prevention programme in Geneva and coordinated the establishment of a comprehensive hepatitis response in the Western Pacific Region. Dr Lo has around 50 publications in peer reviewed Hepatitis & STI, Division literature promoting public health sciences in Asia including in Nature Medicine, Lancet HIV and other reputed international journals. She is an associate editor Diseases, World Health of the Western Pacific Surveillance and Response Journal. Organization, Regional Office for the Western Pacific Region

Dr. Lee graduated MD from Memorial University, Canada, and did residency training at University of Toronto (Internal Medicine and Gastroenterology) from 1978-83. This was followed by a research fellowship in hepatic hemodynamics at INSERM Unit 481 in Paris, 1984-87. He joined University of Calgary in 1988, and is currently Professor of Medicine. He is pastchairman of the International Ascites Club, and former Editor-in-Chief of Liver International. He is currently President of the IASL. He has won numerous teaching and research awards, and has lectured in >35 countries.

He has published >20 book chapters and >230 peer-reviewed papers.
University of Calgary,
Calgary, Canada

Dr. Mahtab graduated from Mymensingh Medical College, Bangladesh in 1995. He did MSc in Gastroenterology from University of London, UK in 1998 and subsequently did MD in Hepatology from Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh in 2006. He is a Fellow of the American College of Gastroenterology. Dr. Mahtab is working as an Associate Professor at the Department of Hepatology, BSMMU. He is also a Visiting Faculty at the Department of Gastroenterology & Metabolism, Ehime University, Matsuyama, Japan.

Professor

Bangabandhu Sheikh
Mujib Medical University,
Dhaka, Bangladesh

1989 MD, State Medical Institute, Mongolia
1998 PhD, School of Medicine, Tokai University, Japan
2008 ScD, Academy of Medical Sciences, Academy of Sciences, Mongolia
2010 Ass. Professor, Mongolian National University of Medical Sciences 2012
Professor, Mongolian National University of Medical Sciences
1989 Researcher, Principal Investigator, Deputy Director, Director, Institute
Professor

Batmunkh Munkhbat
Vice President for Research and Development, Mongolian National University of Medical Sciences

- 2014 – 2015 Director, Science Technology Center, Mongolian National University Medical Sciences
- 2016 Vice President for Research and Development, Mongolian National University Medical Sciences

Clinical and Research Interest:
- Histocompatibility, Immunogenetics, Transplantation Immunology, Human Genetics, Disease Studies and Public Health

Pagbajab Nymadawa
Mongolian Academy of Sciences, “Gyals” Medical Center, LLC, Ulaanbaatar, Mongolia

- 1978-1997: Researcher, Deputy Director for Research, National Institute of Hygiene, Epidemiology, Microbiology, Ulaanbaatar, Mongolia
- 1997-2013: President, Medical Branch, Mongolian Academy of Sciences (later, Mongolian Academy of Medical Sciences),
- Since 2013: Chairman, Board of Directors, “Gyals” Medical Center, Ulaanbaatar, Mongolia.

Clinical and Research Interest:
- Molecular epidemiology of human viral infections
- Ecology of viruses
- Human genogeography

Masao Omata, MD
Yamanashi Central and Kita Hospitals, University of Tokyo, Tokyo, Japan

- 1978-1997: Researcher, Deputy Director for Research, National Institute of Hygiene, Epidemiology, Microbiology, Ulaanbaatar, Mongolia
- 1997-2013: President, Medical Branch, Mongolian Academy of Sciences (later, Mongolian Academy of Medical Sciences),
- Since 2013: Chairman, Board of Directors, “Gyals” Medical Center, Ulaanbaatar, Mongolia.

Masao Omata, MD, has made an effort to revitalize the APASL (Asian Pacific association for the study of the Liver) with Dr. S. Sarin and others for the last 10 years. He is a Co-Editor in Chief of the Hepatology International, an
official journal of APASL. He graduated from Chiba University School of Medicine (Dr. Okuda), and continued his training at Yale University (Dr. G Klaskin) and in the Liver Unit at University of Southern California (Dr. RL Peters). After 6 years in US, he returned to the Department of Medicine at Chiba University in 1989, and started molecular biological study on Hepatitis B virus. In 1992, he became Chairman of Second Department of International Medicine at University of Tokyo, Japan and then subsequently became chairman of Department of Gastroenterology. Under his leadership, the Department of Gastroenterology had become one of the foremost centers in its field. Now, he is the president of the two hospitals at Yamanashi, west of Tokyo, where, although scenic place with Mt. Fuji, hepatitis virus infection is epidemic and his homeland. He and his colleague have published 1,158 articles in English Literature including, NEJM 5, Lancet 6, Ann Int Med 6, Hepatology 59, Gastroenterology 43. The total impact factor is 6,465 and 41,794 citations with H-index of 107 as of March 31st, 2017.

Clinical and Research Interest:
Hepatology, Gastroenterology, Oncology

Education and Career Background:
- Public schools of Delgerkhaan, Jargaltkhaan, and aimag 1-st secondary school of Undurkhaan, 1967-1977
- Biology Faculty of Irkouts state University, Russian Federation, 1982
- Mongolian Medical University, 1984
- Guest scientist, National Institute of Health, Bethesda, Maryland, USA, 1992-1994
- Guest scientist, Institute of Virology, Justus Liebig University, Federal Republic of Germany
- Ph.D (Biol)-1996. Mongolian National University and Mongolian Academy of Sciences
- DR.Sc (Biol)-1998, Mongolian National University and Mongolian Academy of Sciences
- Current research area: Immunobiotechnology of infectious disease agents, particularly viruses

Leading scientist,
Public Health Institute,
Mongolian Academy of Medical Sciences
Education
- Otvos Lorand University, Budapest, Hungary
  - PhD, Genetics, 1983
- Odessa University, Odessa, Ukraine
  - BSc, Biology/Genetics, 1976

Institute of Biology, Mongolian Academy of Sciences
Professor Tsenduren Oyunsuren
Head, Laboratory of Molecular Biology (Feb. 1988-Present)

Member of the
Mongolian Academy of Sciences Laboratory of
Molecular Biology
Institute of Biology
Mongolian Academy of Sciences, Ulaanbaatar, Mongolia

- Leads a team of researchers engaged in studying molecular genetics and molecular biology of different organisms
- Coordinates several research project such as “Genotypes of hepatitis viruses spread in Mongolia”, “Molecular factors cause HCC in Mongolia”, Effects of plant derived components on cancer cell in vitro culture”, In-house production of some diagnostic ELISA kits, “Molecular phylogenetics of hepatitis viruses”, “Host genetic factors for hepatitis virus associated diseases in Mongolia” and others.
- Collaborates with Japanese, Chinese, Hungarian and American researchers.

School of Biology and Biotechnology, National University of Mongolia
Lecturer, professor
- Gived lectures on Molecular Biology, Genetics, Cell Biology, Biotechnology.
- Supervises BSc, MSc & PhD works

Selected Books
- Molecular Genetics I, 2003 and Molecular Genetics II, 2013. (in mongolian)
- Genetic resources and Biosafety, 2006. (in mongolian)
- Biotechnology in Mongolia, 2009. (in mongolian)
- Molecular genetics characteristics of HBV, HDV and HCV spread among the Mongolian population. 2011 (in mongolian)


25. Эллипин эмийн элэгний хорт хавдарын эсийн үйл ажиллагаанд үзүүлэх нөлөө Одгэрэл О, Оюунсүрэн Ц, Эрдэнэбаатар П, Номинтуяа Г, Тэмүүжин Ж, Хүрэлбаатар Л. Монголын Анагаах Ухаан, 2011.

26. Элэгний хорт хавдарын in vitro дахь эсийн үйл ажиллагааг эмийн багваахайгаас (Taraxacum officinale Wigg FH) зарим бодис дарангуйлж буй байдал. Ж. Болдбаатар, Б. Тувshintugs, О. Одгэрэл, Г. Одонтуяа, Р. Сандуйжав, П. Эрдэнэбаатар, Ц. Оюунсүрэн, SHU-ийн мэдээ: 67-78, 1(199), 2011.


Professor Diana Alcantara Payawal
Fatima university medical center, Manila, Philippines

- Fellowship in Hepatology, Interventional Sonology and Digestive Endoscopy and Molecular Biology, Department of Gastroenterology, University of Tokyo, Tokyo Japan through a scholarship Ministry of Education, Japanese Government (MOMBUSHO)
- Fellowship in Gastroenterology and Digestive Endoscopy Unit, Digestive Endoscopy of University of Santo Tomas, Manila, Philippine
- Diploma, Tropical Medicine and Hygiene, Degree School of Tropical Medicine, Mahidol University, Bangkok, Thailand through scholarship Southeast Asia Ministry of Education (SEAMEO)
- Residency Training in Internal Medicine Department of Internal Medicine, Cardinal Santos Medical Center
- Faculty of Medicine and Surgery University of Santo Tomas, Manila, Philippines
Prof Shiv Kumar Sarin is the Senior Professor and Head, Hepatology and Director, Institute of Liver and Biliary Sciences, New Delhi. He was instrumental in setting up the Institute of Liver and Biliary Sciences (ILBS), under the auspices of the Govt of Delhi. He has more than 480 publications to his credit, edited 13 books on liver diseases and contributed 83 chapters in various medical text books. He has helped develop 18 major guidelines; including six major Asian Pacific Treatment Guidelines in Liver diseases. He is credited with several new treatment protocols for liver diseases, specially variceal bleeding, liver regeneration, hepatitis B and acute-on-chronic liver failure.

He is the founding Co-Chief Editor of Hepatology International. Has been a recipient of the highest Award in Science in India, The World Academy of Medical Sciences International Prize, EASL International Recognition Award and ‘Most Distinguished Physician from India” from the American Association of Physicians of India.

Education and Career Background:
1994 Medical Doctor, Medical Science University, 1998 Master of Medical Science, Medical Science University
2009 Refresher Course, Postgraduate Training Institution, Irkutsk, Russia 2010 Doctor of Medical Science, Microbiology-Epidemiological Research Center, Irkutsk, Russia
2015 Clinical Professor, Mongolian National University of Medical Sciences 2015 Doctor Consultant, Board Council on Infectious Disease

Professor Jinsil Seong currently works at Department of Radiation Oncology, Yonsei University College of Medicine, Seoul. She graduated from Yonsei University College of Medicine, Seoul and subsequently completed her PhD degree from Yonsei University. Then she studied as a visiting scientist in M.D. Anderson Cancer Center, Houston, USA. Professor Seong is a former President of Yonsei Liver Cancer Study Group and served as a member of the Editorial Board of International Journal of Radiation Oncology Biology Physics for the past 10 years. Currently she is a president of Korean Liver Cancer Association.
Professor Jinsil Seong

Department of Radiation Oncology, Yonsei University College of Medicine, Seoul, South Korea

and a president of Korean Society of Radiation Bioscience. Internationally, she is secretary general of Asia Pacific Primary Liver Cancer Expert Association, a country-representing board member of Asian Clinical Oncology Society, as well as a consultant in International Atomic Energy Agency.
Professor

Mongolian Academy of Sciences, Shagdarsuren Hospital

Shuichiro Shiina graduated in Medicine at the University of Tokyo in 1982. He completed a residency and fellowship training at the University of Tokyo Hospital and Mitsui Memorial Hospital. He received Ph.D. degree in Medical Science with a study “A randomized controlled trial of radiofrequency ablation with ethanol injection for small hepatocellular carcinoma (Gastroenterology 2005) at the University of Tokyo in 2005. He moved to Juntendo University in December 2012. Dr. Shiina has been a pioneer of image-guided percutaneous ablation therapies for liver tumors, such as percutaneous ethanol injection, percutaneous microwave ablation, and radiofrequency ablation. He has performed radiofrequency ablation on over 10,000 patients with liver tumors at the University of Tokyo and Juntendo University. Dr. Shiina published over 200 International scientific papers in high quality English Journal and over 300 domestic scientific papers. He is a member of The American Gastroenterological Association, Asian Pacific Association for the Study of the Liver, The International Liver Cancer Association, The Japanese Society of Internal Medicine, The Japanese Society of Gastroenterology, The Japan Society of Hepatology, Japan Gastroenterological Endoscopy Society, The Japan Society of Ultrasonics in Medicine, The Japanese Society of Adult Diseases, The Liver Cancer Study Group of Japan, Study Group of Microwave Surgery, The Japan Society of Clinical Oncology, The Japan Pancreas Society, and Japanese Society for Gastroenterological Carcinogenesis, Japanese Society of Interventional Radiology, and others.

His research interests are “Interventional Oncology, such as Radiofrequency Ablation”, “Diagnosis and Treatment of Liver Neoplasms”, and “Chemotherapy of GI tract and Liver Cancers”.

Professor

Juntendo University, Tokyo, Japan
He graduated at Toho university school of medicine in 1992. He worked at Tokyo university hospital during from 1992 to 2008. From 2008, He has been worked in Kyoundo Hospital which is afferent hospital of Tokyo university hospital. His specialty is gastroenterology and hepatology, especially, Minimum-invasive treatment (PEIT, RFA, TAE) for hepatic neoplasms. He has been performed RFA over 2000 patients at Tokyo university and Kyoundo Hospital during 25 years. He also perform hepatic angiography and enhanced ultrasonography.

Professor

Toshiyuki Kawai,
Takafumi Sugimoto, Miho Kanda, Yuji Kondo.
Kyoundo Hospital, Liver Unit, Tokyo, Japan

Professor Internal Medicine. Department Gastroenterology and liver unit; Faculty of Medicine, Mansoura University
Founder and Head of the Association of Liver Patients’ Care (ALPC), Dakahlia, Egypt.
Member of Board of European liver patients’ association (ELPA) (2006-2008)
Founder and CEO of the Egyptian Liver Research Institute and Hospital (ELRIAH).

Professor Gamal Shiha
President of the African Liver Patients’ Association (ALPA)
Hepatology, Gastroenterology, Liver Fibrosis, HCV, HBV

Degree of M.D, Nagoya City University, 1991
Clinical staff at Division of Gastroenterology, Nagoya Daini Red Cross Hospital: 1993 – 1997
Visiting fellow at Department of Transfusion Medicine, National Institutes of Health: 1999 – 2001
Degree of Ph.D, Nagoya City University Graduate School, 2001
Lecturer at Department of Clinical Molecular Informative Medicine, Nagoya
Education and Career Background:

Professor, Department of Virology & Liver unit, at Nagoya City University Graduate School of Medical Sciences, and Sub Director, Liver Disease Unit, Nagoya City University Hospital. 2009-

Director, Central Clinical Laboratory, Nagoya City University Hospital. 2009-

Professor Tawesak Tanwandee MD is hepatologist at Division of Gastroenterology and Hepatology at Siriraj Hospital, Mahidol University, Bangkok, Thailand where he has been working for past 25 years. His current position is Associate Professor of Medicine and Head of Division of Gastroenterology (since 2008). He is also immediate past president of The Liver Society of Thailand, Secretary General of APASL annual meeting 2011 and APDW annual meeting 2012. His research interest is about treatment of chronic hepatitis B and C, hepatocellular carcinoma and cost effective of treating hepatitis B and C in Thailand. He received a MD with first class honor and gold medal for top of the class and received Thai Board of Internal Medicine, Gastroenterology and Family Medicine. He also spent 2 years performing research at Department of Molecular Virology, Baylor College of Medicine, Houston, TX. He is currently member of APASL, AGA, ACG, AASLD, EASL and ILCA.

Clinical and Research Interest:

Chronic hepatitis B and C, hepatocellular carcinoma
Professor Lai Wei
Peking University
People’s Hospital,
Beijing, China

Professor Khin graduated from Mandalay University of Medicine, Myanmar in 1974 and in 1978 obtained Master Degree in Internal Medicine. Trained in GI and Liver Services in Royal Infirmary Edinburgh under Dr Neil Finalyson in 1983 and joined Liver Unit Royal Free Hospital London as assistant lecturer under Professor Dame Sheila Sherlock and Prof Neil McIntyre. He achieved MRCP in 1984 and FRCP in 1997. After completing his studies, he worked at Liver Unit, Yangon General Hospital (YGH) and Head of Department of Hepatitis C and B, NAFLD.
Professor Khin Maung Win

Honorary Professor, Experimental Medicine, Department of Medical Research (DMR). In 1991, received a scholarship as Senior Research Fellow from WHO and worked at Hôpital Henri Mondor, Paris for one year with Jean-Michel Pawlotsky under Professor Daniel Dhumeaux. He was trained in clinical Hepatology as well as bench works on effect of TGF β on Hepatic Stellate cells and was able to publish two-peer-reviewed articles on liver fibrosis. From 1994 to 2007, he served as Professor and Head of Department of Hepatology in YGH. He established GI & Liver Centre and heads the Department of Hepatology in Yangon GI and Liver Centre to date. He involved in many multi-centre trials as Principal Investigator, participating in Investigator initiated trial on ‘Phase III Multi-Centre Open-Label Randomized Controlled Trial of Selective Internal Radiation Therapy Versus Sorafenib in Locally Advanced Hepatocellular Carcinoma’

Clinical and Research Interest:
- Hepatitis B & C, HCC

- 1975 Graduated Chiba University School of Medicine
- 1975-1978 Trainee in Chiba University Hospital (Professor K Okuda)
- 1978-1980 Royal Free Hospital, London (Professor S Scherlock, Professor BH Billing)
- 1980-1985 Fellow (Chiba University) Professor M.Omata
- 1984 Fox Chase Cancer Center, Philadelphia (Dr. J Summers)
- 1985 Degree of Dr. of Medical Science
  - 1985-1994 Assistant Professor, Chiba University
- 1994-2006 Lecturer in Medicine, Chiba University
- 2006- Director and Professor of Medicine, Chiba University
- 2008-2014 Secretary General of APASL
- 2013-2015 Dean, Chiba University School of Medicine
- 2016 President Elect of APASL 2016 Tokyo
- 2016 President of 52nd Annual Meeting of Japan Society of Hepatology
- 2016 Professor Emeritus, Chiba University
- 2016 President of Funabashi Central Hospital
Do Young Kim is now a professor of Internal Medicine at Yonsei University College of Medicine, Seoul, Korea, and a hepatologist in the Severance Hospital where he has been a faculty member since 2007. He graduated Yonsei University at 1996, and completed training course in Severance Hospital from 1996 to 2001. He studied proteomics and microRNA in hepatocellular carcinoma (HCC) at Fred Hutchinson Cancer Research Center as a research associate between 2011 and 2012. His main research interest is novel treatment of advanced HCC such as transarterial radioembolization and immune-oncology. He is one of the investigators in several clinical trials related to molecular target drugs for HCC. He published approximately 150 international original articles, and is an academic editor of PLoS ONE, Yonsei Medical Journal and World Journal of Hepatology. He also acts as a reviewer of Liver International, Gut and Liver, Molecular and Clinical Hepatology, and Journal of Korean Medical Sciences.
Ming-Lung Yu, MD, PhD, is a Distinguished Professor at the College of Medicine, Kaohsiung Medical University, Taiwan. Professor Yu graduated from the College of Medicine at Kaohsiung Medical University in 1989 before going on to obtain a PhD from the Graduate Institute of Clinical Medicine in 2000. Professor Yu, a board-certified internist and gastroenterologist, is currently teaching at the Kaohsiung Medical University and Kaohsiung Medical University Hospital where he is holding the leading role of Hepatitis Center and Hepatobiliary section, Department of Internal Medicine. Currently, he is also a Visiting Professor at Liver Center, Division of Gastroenterology, Massachusetts General Hospital, Boston, MA, USA.

Endowed Professor in Medicine of the Li Shu Fan Medical Foundation, the Chief of the Division of Gastroenterology and Hepatology, the Deputy Head of University Department of Medicine, The University of Hong Kong, the Deputy Chief of Service of the Department of Medicine, Queen Mary Hospital, Hong Kong and the Assistant Dean of the Faculty of Medicine, the University of Hong Kong. Professor Yuen is also serving as an editor for several international medical journals as well as a reviewer for many high impact factor journals, including New England Journal of Medicine, Lancet, Lancet Infectious Diseases, Gastroenterology, Gut and Hepatology etc. Professor Yuen has published more than 350 papers in world renowned medical journals.

Prevention, natural history, molecular virology and treatment of chronic hepatitis B and C, and hepatocellular carcinoma.
Professor Cihan Yurdaydin specialized in Internal Medicine at the University of Ankara Medical School, Turkey, after gaining his medical degree from the same establishment. After a year of national service at Gümüssuyu Military Hospital and two years at Van State Hospital, he returned to the University of Ankara Medical School to specialize in gastroenterology. Dr. Yurdaydin has worked for one year on hepatic encephalopathy at the University of Vienna, Austria and was a visiting fellow at the Liver Diseases Section of the National Institutes of Health between 1991 and 1993. Professor Yurdaydin currently is Professor of Gastroenterology at the University of Ankara Medical School and is also Chief of the Hepatology Institute, University of Ankara. Professor Yurdaydin was an Editorial Board member of the Journal of Hepatology from 1995 to 2000 and has been Editor-in-Chief of The Turkish Journal of Gastroenterology from 1999 to 2013. He was an associate editor for Liver International from 2007 to 2012. Professor Yurdaydin has published in peer reviewed journals such as the NEJM, Nature Reviews, Gastroenterology, Hepatology and Journal of Hepatology. He co-organized 2 EASL Monothematic Conferences in Istanbul, one on hepatitis B and the other on hepatitis Delta. An active member of the AASLD, EASL and Turkish Society for Gastroenterology, Professor Yurdaydin is also a member of the Turkish Association for the Study of the Liver and the Turkish Transplantation Society. He was an Executive Member of ASNEMGE and has served in the Scientific Committee of EASL. Professor Yurdaydin was Educational Councilor to EASL from 2013 to 2015 and is currently serving as president-elect for the World Gastroenterology Organization.

Hepatitis B and hepatitis D, hepatic encephalopathy
Friday, June 16, 2017

OFFICIAL SYMPOSIUM I

Real-World Experience of HCV Treatment and National Program of Viral Hepatitis in Asia-Pacific Region

Chairs

Professor Jazag Amarsanaa
Scientific Committee Chairman

Professor Barjesh Chander Sharma
Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Professor Diana Alcantara-Payawal
Fatima University Medical Center, Manila, Philippines
Hepatitis C virus (HCV) is the most common serious liver infection in the world as well as in Armenia. 3% of the world population is infected with HCV and infection leads to progression of liver diseases, including hepatic cirrhosis and hepatocellular carcinoma (HCC). HCV infection is characterized with the geographical distribution as having high, intermediate and low levels of infection. According to initial statistical data Armenia is the country with intermediate prevalence of HCV infection, because >4% of Armenian general population is infected with HCV. Data on HCV infection in Armenia are limited. The serological screening was carried out among above 10000 persons, including healthy population (blood donors, pregnant woman, conditionally healthy persons) and different risk groups for parenteral viral hepatitis (injecting drug users, healthcare workers, patients with sexual transmitted infections, oncological and oncohematological diseases, tuberculosis, hemodialysis patients, special contingent in prisons). According to our data among healthy population the presence of anti-HCV was 3.6±0.5%. Anti- HCV prevalence was 6.1±0.8% among oncohematological patients, which is higher, than in solid tumor patients (3.1±0.2%). There was a high prevalence of anti-HCV among injecting drug users (64.0±1.9%), special contingent of the penitentiary institutions (36.3±2.3%), hemodialysis patients (29.4%). Positive results for anti-HCV were found among patients with sexual transmitted infections, tuberculosis, health care workers in 10.2±1.2, 9.0±1.3, 6.8±0.8%. These risk groups have the main role in maintaining the intensity of epidemic process for HCV in the country. The epidemiology of HCV infection has changed during the past decade and main modes of transmission of HCV infection are I/V drug using and medical procedures instead of hemotransfusion.
Myanmar is a country with high incidence of chronic Hepatitis C infection (2-4%). Genotype distribution of HCV infection in Myanmar is Genotype 3 (41%), Genotype 6 (36%), Genotype 1 (22%), Genotype 4 (3%) and Genotype 2 (1%). Unique feature of genotype distribution in Myanmar is high prevalence of genotype 6.

In the era of direct acting antivirals (DAAs), literature of treating genotype 6 patients with DAAs are very scarce and sample sizes of the studies are very low. Therefore it is expected that this study with real life data on 174 patients will be great contribution to the understanding of treatment of genotype 6.

Method
The data of chronic HCV patients with genotype 6 treated at Yangon GI and Liver Center from 1st December 2015 were analyzed to know the safety and efficacy of generic DAAs therapy. According to the published international guidelines, choice of DAAs and duration of therapy were determined by degree of fibrosis. However, in Myanmar the choice of the DAAs heavily depends on the availability of DAAs and financial status of the patients. HCV viral load is assessed at the baseline of treatment, week 4, week 8, week 12, week 24 and SVR 12.

Results
Of the 177 Genotype 6 patients treated with different DAAs based therapy; 1. SOF/PegIFN/RBV 12 (44), 2. SOF/RBV 24 (24), 3. SOF/LED 12 (78), 4. SOF/LED and RBV 12 (12), 5. SOF/LED 24 (7), 6. SOF/LED and RBV 24 (12). 58% female, age from 17 to 83 with mean age of 52.91, mean BMI is 22.36 (range from 15 – 40). 147 patients (83%) are treatment naïve, 30(17%) treatment experienced (PegIFN/RBV) and mean HCV RNA is 4,238,154.12 IU/ml. The overall SVR 12 rates were 85.31% (151/177). SVR12 rate of treatment naïve was 82.3% (121/147) and 100% (30/30) in treatment experienced patients. The common adverse events were fatigue, headache and insomnia in PegIFN based regimen. No patients discontinued treatment due to adverse events.

Conclusion
According to real life experience of treating HCV patients in Myanmar by different Sofosbuvir based regimens, the SVR rate were SOF/PEG/RBV 12
Compared to other genotypes in Myanmar, genotype 6 is found to be most difficult to treat genotype comparing to SVR rates (above 90%) in other genotypes. However, with addition of either PEG or RBV to SOF, the efficacy is increased to 100% indicating that either PEG or RBV is necessary for higher efficacy of SVR rates.

Substained virological response
Friday, June 16, 2017 08:20-08:30

Professor

Peking University

People’s Hospital, Beijing, China
Friday, June 16, 2017 08:30-08:40

Speaker

OS 1 - 4: Real-World Experiences of HCV Treatment, and
With emergence of new prevalence studies about 210,000 people (approximately 7%) are now HCV RNA (+) in Mongolia. After all-oral DAA was introduced in our country, total of more than 12,000 patients were enrolled in anti-HCV treatment.

Mongolia was one of first countries from the developing world to start (Dec, 2015) the all oral treatment. So the countries from around the world are carefully watching our progress.

Since the start of treatment, many new unexpected side effects and adverse events were registered during 3-6 months of LED/SOF treatment course. I will introduce those events in my presentation. HCV genotype distribution is not a barrier for treatment inclusion, because over 98% of HCV infected patients have Genotype 1b. And treatment result is very good, over 96% of SVR rate. We will share our real-life experiences with other countries.

With the new “Liver disease Prevention, Control and Elimination Program” approved by the parliament, our government is planning to eliminate HCV by 2020, which is quite an ambitious plan. But it is better to have overly ambitious plan, than dragging the end date for too long. Some flaws still exist in national program such as lack of baseline statistics, but we hope it will be done in the first few years of implementation.

Stage one of population-wide screening (40-65 year old) for serum HCV-Ab and HBsAg has started this year.

Even with health insurance coverage of most treatment costs, geographical sparsity, income disparity, cost of diagnostics, level of disease awareness are main reasons of lower than expected patient turnaround.

We still fear “hole in the bucket” phenomena, because of lack of heavy investment in hospital sanitation and disinfection. We need more investment or proper business conduct support for small dental offices, which are considered as one of main sources of new HCV infections.

In conclusion, we are one of leaders in the region on HCV elimination progress, enrollment, policy and strategy development at both national and subnational level.
Hepatitis C in Turkey is mostly secondary to infection with hepatitis C virus (HCV) genotype 1. 95% of HCV patients in Turkey are infected with genotype 1, around 85% genotype 1b and 10 % genotype 1a. The rest is due to genotypes 2, 3 and 4. An exception to this general genotype distribution is a region in Central Turkey where genotype 4 prevalence was much higher. All oral combination treatment is available for treatment of HCV patients since July 2016 in a restricted way limited to treatment non-responder patients and treatment naïve patients with cirrhosis. Indications to treatment have been extended in March 2017 to all treatment naïve patients except those with fibrosis grade 0 on liver biopsy, i.e. including patients with grade 1 fibrosis. Treatment with ledipasvir/sofosbuvir (L/S) and ombitasvir/paritaprevir/ritonavir/dasabuvir with ribavirin (O/P/R/D- R) is licensed and fully reimbursed for the treatment of HCV. The insurance body in Turkey is basically the state and full instructions regarding treatment is given by the insurance body. If patient and physician wants to use a treatment regimen outside these instructions treatment is not reimbursed. Genotype and HCV RNA determinations are prerequisites for treatment. In genotype 1 patients, who were non-responder to a previous treatment regimen consisting of pegylated interferon-ribavirin (Peg/R) both L/S ± R or O/P/R/D ± R can be prescribed with some treatment regimen restrictions described below. With L/S treatment duration is 12 weeks when R is given concomitantly and it is 24 weeks without R addition irrespective whether HCV genotype is 1a or 1b. With O/P/R/D treatment duration is always 12 weeks. However, in genotype 1a patients treatment includes R whereas in genotype 1b patients R is not included. In patients who were nonresponder to treatment with P/R with telaprevir or boceprevir only L/S ± R can be prescribed. No treatment regimen is reimbursed for all oral treatment non-responders. In P/R treatment experienced patients who do not have decompensated cirrhosis either L/S or O/P/R/D can be given. In treatment naïve patients, a liver biopsy is required except patients with decompensated cirrhosis or who have a contrindication to liver biopsy. In patients with grade 0 fibrosis treatment is not reimbursed. In non-cirrhotic genotypes 1 patients only O/P/R/D ± R is reimbursed. Cirrhosis is defined as having a Ishak fibrosis score of 4 or greater on liver biopsy. In compensated cirrhosis both L/S ± R or O/P/R/D ± R and in decompensated cirrhosis only L/S ± R can be prescribed. More than 800 patients have been treated so far in Turkey with all oral combination treatments consisting of the 2 regimens described above. No significant safety issues have been observed and the overall sustained viral response rate appears to exceed 95%.
In India prevalence of hepatitis C virus (HCV) infection is 0.9%-1.9% with much higher prevalence in some areas of northeast India, in some tribal populations and some parts of Punjab. HCV RNA is detectable in 80% of anti-HCV positive subjects. HCV genotype distribution in Indian patients demonstrates prevalence of genotype 3 in 62% and genotype 1 in 31% cases. There are approximately 12-18 million HCV infected individuals in India. The prevalence of IL28b genotype CC/CT/TT is 61.1%; 30.5%; and 8.4%, respectively. The nonCC genotypes are significantly higher in non-responders compared to responders. For genotype 1-infected patients, peginterferon α-2a/2b plus ribavirin for 48 weeks results in 40-52% sustained virological response (SVR) rates in treatment-naive patients. For genotype 3 and 2-infected patients, peginterferon α-2a/2b plus ribavirin for 24 weeks leads to 70-80% SVR rates. In patients who do not achieve a rapid viral response (RVR) with combination of peginterferon and ribavirin, an extended course up to 48 weeks is used for genotype 3 and 2. Noncirrhotics have better SVR rates compared to cirrhotics treated for same duration. Factor associated with SVR are age < 40 years, absence of cirrhosis, RVR and no reduction in interferon dose. Side effects and cost related to these drugs are important concerns in India where patients have to bear their health expenses. SVR is seen in 70% of patients and IL28b genotype CC/CT/TT distribution is 61%, 31% and 8% respectively. The non-CC genotypes are significantly higher in non-responders compared to responders (68% vs. 39%). CC genotype is independent factor predicting SVR in patients infected with genotype 3. IL28b CT/TT genotype correlates with treatment non-response in patients infected with genotype 3. Treatment of hepatitis C has been revolutionized with arrival of directly-acting antivirals (DAAs) since March 2015. Sofosbuvir has been approved by FDA for genotype 3 and also licensed in India. Recently in India prices of sofosbuvir has fallen considerably to a level that low and middle income status patients can afford. Combination of sofosbuvir and ribavirin for 24 weeks for genotype 3 has achieved more than 90% of SVR rates. NSSA inhibitor daclatasvir and ledipasvir has been recently approved and available in India and may further improve outcomes especially in advanced cirrhotics, patients with renal failure and post liver transplantation. Daclatasvir is pan-genotypic whereas ledipasvir is effective in genotype 1 and 4. Role of DAAs has not been fully evaluated in treatment naive, non-responders and relapers in genotype 3 patients. There is urgent need for large clinical trials using DAAs and host modulators in patients with genotype 3 infection. Phase 3b trial on efficacy of sofosbuvir is going on and results are awaited. Educating and increasing the awareness of the public and medical personnel regarding HCV and emphasizing the importance of safe blood and injections is required for the control of infection. Screening of high risk population, health awareness and education, increasing treatment efficacy (DAA) and securing the access to treatment are the few important steps for control and prevention of HCV infection.
Pakistan has the 2nd highest burden of HCV infection in the world after China, Professor with an estimated 10 million infected persons based on a national prevalence rate of 5%. To counter this huge disease burden, various government programs have run at the federal and provincial level. However the performance of these Aga Khan University, programs has been dismal and therefore a revised “National Hepatitis Strategy Karachi, Pakistan 2017-21” will be finalized very shortly.

Pakistan was a beneficiary of the global access program for DAAs, through which Sofosbuvir was introduced into the country in 2014 followed by generic licensing in 2015. This has created an upsurge in treatment, mainly in the private sector, so that currently close to 100,000 patients are treated each year. However most treatment has been with SOF and Riba combinations, which has required six months of therapy as genotype 3 is our predominant infection. Nonetheless SVR rates with this combination alone are excellent and yield better results in the real life compared to those in the pivotal trials, particularly for cirrhotic patients both naive and IFN treatment experienced.

With the advent of Daclatasvir and Epclusa in the coming months, shorter pan genotypic regimens will become the standard therapy. This is coupled with governmental efforts to significantly enhance treatment rates in the next fiscal year.
In Mongolia, there is a phenomenon of absolute dominance of 1b virus genotype of - 98.8% (Baatarkhuu O. et al., 2008). In ethnically close Buryatia, its concentration does not exceed 54.8% (Malov S.I. et al., 2012), and in neighboring China - 56.8% (Gower E. et al., 2014). A possible explanation for the existing phenomenon may be the presence of a genetic predisposition of the population to the 1b genotype, in which this clone of the virus receives a selective advantage when distributed in Mongolia. The aim of this study was to test the proposed hypothesis by the study of the SNP genes IFNL4 (rs368234815), IFNL3 (rs12979860 and rs8099917), CD209 (rs4804803), TLR3 rs3775291 and rs13126816 in cohorts of Mongolian patients with hepatitis C virus and in the ethnically similar Buryat group, and also in patients with Hepatitis C caused by different virus genotypes.

Methods and Result:
A total of 400 patients with chronic HCV were examined, including 200 from the Republic of Buryatia and 200 from Mongolia. The compared groups of patients completely matched in clinical-laboratory and sexage indices. There were no associations of polymorphic variants of the genes CD209, IFNL3, and ethnicity of patients, as well as genotypes of the virus in the Buryat population. Obviously, the internalization of different genotypes of the virus into the cell is universal, and, at least, does not depend on the polymorphism of the CD209 gene. In contrast, as a result of the work performed, two SNPs in the candidate genes TLR3 (rs3775291) and IFNL4 (rs368234815) were detected, polymorphic variants of which occur with different frequency in patients with 1 and not 1 (2/3) genotypes of the virus. Carriers of G-allele rs3775291 TLR3 are 3.1 times more resistant to infection with 2/3 virus genotypes (p <0.0001), and carriers of ΔG-allele rs368234815 IFNL4 - 2.0 times (p <0.02). Consequently, the higher the proportion of human carriers of these alleles and their haplotypes in a population, the higher the tolerance for the spread of 2/3 genotypes of the virus in it. Under these conditions, the first genotype of the virus will receive genetically determined selective advantages, displacing the 2nd and the 3rd from circulation.

Conclusion:
Further studies at the level of practically healthy people in Mongolia and Buryatia, as well as the inclusion of other polymorphisms in the analysis will help establish the role of congenital immunity genes in the selective selection of individual genotypes of the virus. The study was carried out with the financial support of the RFBR grant No. 16-54-44047.
**APASL Single Topic Conference 2017**

**6th HCV Conference**

**16 - 18 June • Ulaanbaatar • Mongolia**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:30</td>
<td>Opening ceremony</td>
</tr>
<tr>
<td>09:45</td>
<td>Welcome Speech by President of the APASL STC 2017, 6th HCV Conference Professor Oidov Baatarkhuu</td>
</tr>
<tr>
<td>09:55</td>
<td>Welcome Speech by TBD</td>
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<tr>
<td>10:05</td>
<td>Welcome Speech by Minister of Health Dr. Ayush Tsogtsetseg</td>
</tr>
<tr>
<td>10:15</td>
<td>Welcome Speech by Coordinator, HIV, STI, viral hepatitis unit, WHO WPRO Dr. Ying-Ru Lo</td>
</tr>
<tr>
<td>10:20</td>
<td>Welcome Speech by Chairman of the Scientific Committee of the APASL STC 2017, 6th HCV Conference Professor Jazag Amarsanaa</td>
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Viral hepatitis B and C are one of the major causes of liver cirrhosis and HCC worldwide. The 69th World Health Assembly has approved the Global Health Sector Strategy to eliminate HCV infection by 2030, which can become a reality with the recent launch of direct-acting antiviral therapies.

In 2015, 71 million persons worldwide are living with HCV infection. Overall, in 2015 the global prevalence of HCV infection was 1.0%. Genotypes 1 and 3 were the most common causes of HCV infection worldwide.

Conversely, among all global HIV-infected persons, the prevalence of anti-HCV was 6.2% (Lancet 2015).

In 2015, the global prevalence of HBV infection in the general population was 3.5%. Prevalence was the highest in the African 6.1% and Western Pacific regions 6.2%. Overall; about 257 million persons were living with HBV infection.

Mongolia is a developing country, located in central Asia. The total population of Mongolia as of July 2015 is estimated to be 3.1 million people ranking at 138th in world population. Mongolia is a unique country with high endemicity for three blood-borne hepatitis viruses, namely HBV, HCV, and HDV. Viral hepatitis B and C are one of the major causes of liver cirrhosis and HCC in Mongolia. 92-95% of HCC cases in Mongolia are related with HCV and HBV co-infections and occurring as 115 cases per 100,000 people per year. However, HCV and co-infections are still one of the serious public health concerns in Mongolia.

I will discuss HCV and co-infections based on several published studies conducted in the last decade.

1. We have completed the study named “Prevalence and genotype distribution of hepatitis B and C virus among apparently healthy populations.
in Mongolia: a population-based nationwide study”. This study population consisted of 1512 subjects from 13 provinces and Ulaanbaatar, capital of Mongolia, aged from 0 to 80 years. According to our study results, the prevalence of anti-HCV was 15.6%, 11% of which was detected to be HCV RNA positive. In addition the prevalence of HBsAg was 11.8%. Therefore, we can say that the prevalence of HBV and HCV infections is very high in Mongolia.

The prevalence of anti-HCV and HCV RNA had a tendency to increase with age. The prevalence of antiHCV and HCV RNA in the population aged over 61 years was significantly higher than those aged 31 to 40 years among this study.

The history of dental care, surgery, and tattooing was significantly more frequent in anti-HCV positive subjects compared with anti-HCV negative subjects.

Here you can see the results of our study on genotype distribution of Hepatitis C in rural and urban areas of Mongolia. Interestingly, the most of HCV infection is caused by genotype 1b. On the other hand, genotype 2 of HCV is very rare, less than 2 percent in Mongolia. The extreme predominance of HCV genotype 1b in the Mongolian population can be explained by the greater ethnic and genetic homogeneity of the current Mongolian population.

The second study is a baseline survey of a Nationwide Cancer Cohort Study. Population based national cross-sectional survey was conducted with multistage random cluster sampling. A population aged 10-64 years in Metropolitan area and 4 geographic regions were randomly selected. Among study subjects 37.2% were from rural provinces and 39.2% were men. The prevalence of HBsAg was 10.6%. Additionally, HCV infection was observed in 9.9% and 0.8% were co-infected with HBV and HCV.

The third study investigated the population-based prevalence of HBV and HCV infection prevalence among apparently healthy population in Ulaanbaatar city of Mongolia.

2667 people who live in Ulaanbaatar were included in this study. The rapid immunochromatographic test was applied for detection of HCV antibodies and HBV rapid test.

The mean age of the subjects was 38 ± 12 years, and 1064 (51%) were male. The anti-HCV prevalence was 9% (n = 185). In addition, the prevalence of HBsAg was 8% (n = 166). The median age of HBV infection was 39 ±12.

Overall, according to the 2008 study conducted by Dr. O. Baatarkhuu, the prevalence of anti-HCV in Mongolia was 15.6%, and HBV was 11.8%. In the 2015 to 2016 studies conducted by Dr. D.Davaalkham and Dr. J. Amarsanaa the prevalence decreased from 9.9% to 9% and HBV decreased from 10.6% to 8% in apparently healthy population.

The previous study included 110 consecutive patients who contracted acute hepatitis in Mongolia and their age ranged from 16 to 48 years. 7 patients or 6.4%, who were positive for both anti-HCV and HCV RNA and negative for the other hepatitis virus markers including anti-HAV IgM, and anti-HBcAgM was tentatively diagnosed as having AHC. Among all HCV RNA positive samples, 100% was classified into genotype 1b.

We undertook time trend analyses between our initial study published in 2005 and the present study between 2012-2014. We sought to investigate changes in the proportion of acute viral hepatitis types in Mongolia over the last decade. The cohort comprised of 546 consecutive patients clinically diagnosed as 50.9%, 26.2%, and 6.0% by cohort. Notably, 16.8% had a dual infection. The etiologies of acute viral hepatitis varied in age groups. The most common cause of acute viral hepatitis among 2-19 year-olds was hepatitis A, and among 20-49 year-olds was HBV and superinfection with HDV and HCV among 40-49 year olds. Patients
with more than one hepatitis virus infection, were significantly older, more likely to be male and had a higher prevalence of all risk factors for disease acquisition. These patients also had more severe liver diseases at presentation compared to those with mono-infection. Acute viral hepatitis is still prevalent in Mongolia. Thus, the need for proper infection control is increasing in Mongolia.
Among the patients with chronic liver diseases, the dual infection of HBV and HDV is 27%, the triple infection of HBV, HCV and HDV is 30%. Of particular note, the triple infection was found in 63% of the patients with HCC and was significantly more frequent than among patients with chronic hepatitis and liver cirrhosis.

According to 2016 national statistics of Mongolia, liver cancer is the most prevalent malignancy which is equal to 44.0% of all cancers in Mongolia. This study population consisted of 195 subjects from 4 hospitals in Ulaanbaatar and the age ranged from 30 to 86 year-olds. The risk factors associated with HCC development were history of acute hepatitis, chronic hepatitis and the presence of liver cirrhosis. The most common etiology for HCC in our patients was HCV infection which is 46%, HBV infection 34%, co-infection B and C 14% and alcohol which is 6.0%. In Mongolia HCC treatment modality is very limited. According to the results of our study, 14% of patients received surgical resection, and their survival was the best. 11.8% of patients received RFA and their survival was 11 months. Approximately 55% of patients received TACE and their median survival was 17 months. The prognosis for patients with supportive care was very poor with a median survival of 5 months. Approximately 20% patients died of HCC progression and the others died of liver failure and GI bleeding.

The National Strategy on Viral Hepatitis Control was approved by Minister of Health in 2010. This strategy was continued for five years between 2010 and 2015. The overall goal of the strategy is to decrease viral hepatitis morbidity to 10 cases per 10,000 populations by 2015. Also the main objective is to control viral hepatitis B and C, and decrease HBsAg carrier rate to 2% among children under 5 year-olds. Mongolia has started to report viral hepatitis since 1952, officially. Approximately 540,000 cases of acute viral hepatitis was reported in the country for past 60 years.

Recently, the Parliament of Mongolia officially approved the implementation of the Hepatitis Prevention, Control and Elimination Program between 2016 to 2020. The current mission of the Hepatitis Prevention, Control and Elimination Program is to eliminate HCV in Mongolia by 2020 and to significantly decrease the incidence of viral hepatitis, liver cirrhosis and HCC. The government of Mongolia allocated 232 billion Mongolian tugrug or 96 million USD for the Hepatitis Prevention, Control and Elimination Program through 2020.

- To screen hepatitis B and C among general populations among 40-65 years old (2017)
- To screen hepatitis B and C among general populations among 15-40 years old (2018)
- Treatment campaign- 12000 have been treated with brand Harvoni and generic Harvoni. Since 2016, there were 4 generic companies and brand Gilead company manufacturing HCV DAAs in Mongolia and branded SOF/LDP price is 300$ per month and generic SOF/LDP price is 150$ per month.

By the end of 2016, the Mongolian Government has included HBV and HCV medicines in the national health insurance, which covers 98% of the population. Therefore, the health insurance will provide 85$ for the brand Harvoni and 65$ for the generic Harvoni.
As of 2017, in the first 5 months approximately 11800 people have been treated by the new DAAs. The cure rate for treatment of HCV infection was 95-99%.
OFFICIAL SYMPOSIUM II

Real-World Experience of HCV Treatment and National Program of Viral Hepatitis in Asia-Pacific Region - II

Chairs

Professor Batarkhuu Oidov
Department of Infectious Diseases, Mongolian National University of Medical Sciences

Professor Saeed Sadiq Hamid
Aga Khan University, Karachi, Pakistan

Professor Lai Wei
Peking University People’s Hospital, Beijing, China
Friday, June 16, 2017 11:10-11:20

10 N h y h S y h y y S y

The WHO estimates that almost 40% of global mortality is due to Chronic viral hepatitis which occurs in the Western Pacific Region. According to the WHO data in May 2014 Liver Disease Deaths in Philippines reached 10,388 or 1.99% of total deaths. Viral hepatitis is the seventh leading cause of death globally, claiming 1.45 million lives in 2013. The Western Pacific Region has only a quarter of the world’s population but bears 40% of global deaths from viral hepatitis, with more than 1500 lives lost each day. The age adjusted Death Rate is 15.58 per 100,000 of population ranks Philippines #87 in the world.

Liver cancer is the 3rd leading sites for both sexes. It ranks 2nd among males and 9th among females. In 1998, an estimated 5,249 new cases, 3,906 cases in males and 1,343 cases in females, and about 4,403 deaths are expected to occur every year. The incidence in males is practically 2 ½ that of females with the Incidence increasing at age 40. Hepatitis B and C infections lead to chronic liver disease, which is the most common causes of liver cirrhosis and liver cancer. The Department of Health estimates that 10% to 16% of Filipino adults or about one in seven adults, suffer from chronic hepatitis B infection. It is also approximated that around 1% of the estimated 100 million Filipinos has chronic hepatitis C. Experts from the Department of Health (DoH), the National Institute of Health, and the World Health Organization (WHO) in the Philippines convened in 2005 to review the current situation of hepatitis in the country. The Regional Action Plan for Viral
Hepatitis in the Western Pacific 2016–2020 provides Member States with tools to reduce viral hepatitis and related liver disease. The action plan was developed through a series of Member State and expert consultations in high-burden countries and at the regional level. The participants agreed to develop a National Hepatitis Action Plan as one of the cornerstones in understanding the true burden of chronic viral hepatitis in the Philippines. By 2012, the Region as a whole—as well as 30 of the 37 countries and areas—were estimated to have met the 2012 milestone of less than 2% chronic hepatitis B prevalence among 5-year-old children. Building on these gains, the Regional Committee in 2013 set a target date of 2017 to reduce chronic hepatitis B infection rates to less than 1% among 5-year-old children—a goal that will ultimately save millions of lives.

Efforts to raise disease awareness in the Philippines have increased the number of cases and patient pool available for hepatitis C treatment. Screening and detection efforts by the Red Cross as well as growing awareness in the Philippines have been largely responsible for the rise in the number of diagnosed cases. These campaigns have encouraged people, mostly from the
urban areas, to opt for physical examinations that enable the detection of hepatitis C. The Hepatology Society of the Philippines has embarked on B-aware campaign whose main task is to increase cognizance of the burden of this disease in health care.

Physicians and key opinion leaders believe that the diagnosis rate will increase gradually, after the Philippine Government officially implements its hepatitis C program to spread awareness of the disease in the country. In the future, refined versions of current hepatitis C virus (HCV) drugs, oral formulations of small molecule inhibitors, and the new drug class known as protease inhibitors are expected to improve treatment success rates for patients and take the market forward. The estimated cost of hepatitis treatment and management in the Philippines can be prohibitive, given that the urban minimum daily wage is at P450 (10 USD). “Hepatitis B profile costs P1,800 (38 USD); ultrasound, P450 (10 USD); hepatitis B viral load, P4,500 (90 USD); viral load for hepatitis C, P6,500 (130 USD); and genotyping, P14,350 (287 USD). Hepatitis B medication costs P135 (3 USD) a day or P49,000 (1000 USD) a year which maybe lifetime. Hepatitis C treatment costs P732 (10 USD) per day for at least three months. Presently only Sofosbuvir is available with combination drugs being available in time. However, these medicines remain expensive and out-of-reach for most in need. The costly prices for hepatitis C medicines, in particular, are a barrier to access across the Region and a pressing issue taken up by government. The highest patient group for Hepatitis C in the Philippines is injecting drug users who share needles both for narcotic and therapeutic purposes. Another patient group at risk for Hepatitis C includes those who receive blood products that may not have been screened properly; the latter is more of a concern in rural rather than urban areas in the country.

One notable aspect of the challenge the onslaught of hepatitis is the presence of laws which continue to give teeth to the monitoring programs and more power in the implementation of the vaccination program against hepatitis B. From 1992, the nationwide immunization program started, to which the hepatitis B birth dose vaccination was included beginning 2006. PhilHealth, the country’s version of a public or national health insurance program, also incorporated hepatitis vaccination in its newborn care package. The local government units are already integrating Chronic Viral hepatitis education in their information campaign that are usually integrated to their HIV programs and are implemented of varying degrees.

The interferon (IFN)-based treatment of chronic hepatitis C virus (HCV)
HCV infection in has begun since 1986. The “standard-of-care” of IFN-based therapy, 48 weeks and 24 weeks of pegylated IFN (Peg-IFN) plus ribavirin (RBV) could attain SVR rates of 70%-75% for HCV genotype 1 (HCV-1) and 85%-90% for HCV-2 patients, respectively. Furthermore, introduction of response-guided therapy that 24 weeks for HCV-1 with lower baseline viral loads (LVL, HCV RNA < 400,000 IU/ml) and a rapid virologic response (RVR, undetectable HCV RNA at treatment W4) and to 16 weeks for HCV-2/3 with a RVR could provide equal efficacy to “standard-of-care (SOC)”. Interleukin-28B genetic polymorphisms have been associated with treatment efficacy with IFN-based treatment for HCV-1 patients, and might be useful in guiding HCV1 therapy.

The Taiwan Health Insurance Administration has begun to reimburse Peg-IFN plus ribavirin therapy for chronic hepatitis C patients since 2003: 24 weeks of Peg-IFN/RBV for patients with RVR, while 48 weeks of Peg-IFN/RBV for patients without RVR, irrespective of viral genotype. Treatment should be stopped at week 16 if patients do not achieve an early virological response (EVR, 12-week HCV RNA decline > 2 logs from baseline).

Currently, there are several IFN-free regimens available in Taiwan, including sofosbuvir plus weight-based dose of RBV, daclatasvir plus asunaprevir, PrOD regimen (co-formulated paritaprevir/r [NS3/4A PI boosted by ritonavir]/ Ombitasvir and Dasabuvir) with/without RBV, sofosbuvir/ledipasvir/Elbasvir/ grazoprevir, and elbasvir/grazoprevir. However, The Taiwan Health Insurance Administration only reimbursed daclatasvir plus asunaprevir and PrOD regimen for the treatment of genotype 1b and 1, respectively, with advanced fibrosis (F3/4).

Fortunately, the Taiwan government set up a central office for the control of HCV in 2017, aiming to eliminating the virus by 2030. The real world data and strategy of HCV elimination of Taiwan will be discussed in the session.
Friday, June 16, 2017 11:30-11:40

Hepatitis C infection (HCV) in Thailand has a significant health impact.
with more than 1% of general population reportedly hepatitis C viremic. These patients will eventually develop chronic liver disease, cirrhosis and hepatocellular carcinoma. Studies in the past have shown that the most important risk factors include exposure to blood or blood products and history of intravenous drug user. After introduction of universal blood donor screening in 1991 by anti-HCV first then combination of anti-HCV and nucleic acid testing (NAT), blood transfusion related HCV is very rare. Moreover, the shrinkage of intravenous drug users in Thailand since they change their behavior to use amphetamine instead, this even further reduce the incidence of new infection. Currently most of HCV cases are in the age range of more than 50 years old and recent mass survey in 2014 had shown the incidence of viremic HCV of just 0.39%, much lower than previous survey in 2004. Distribution of HCV genotype in Thailand leads by genotype 3 of more than 50%, follow by genotype 1 and 6. Regarding HCV treatment, conventional interferon/ribavirin then pegylated interferon/ribavirin has been the main treatment for decades. Originally is was reimbursed only in government employees until in 2013 when the treatment can be reimbursed for all Thai citizens with evidence of significant fibrosis. The result of peginterferon/ribavirin treatment was similar to the response in Asian which was higher than that in western countries in all genotypes. We are in the preparation to move from interferon-based regimen to all oral regimen which will be implemented soon. Real-world result of all oral regimen including sofosbuvir/ledipasvir or sofosbuvir/daclatasvir for 12 weeks had shown promising result with sustained virological response at week 12 almost 100%. Recently, we have done cost-effective analysis showing that all oral regimen is more cost-effective than peginterferon-based regimen, even cost saving.

Last year, it was the first time that we had responsible body to control the policy of hepatitis and ministry of public health of Thailand has set to policy to treat HCV case at least 50% more in the next 5 years. This program must include case finding, treatment networking to setup simplify treatment guideline so that practitioner can treat by following the guideline and provide the treatment with all oral regimen. However, we still do not have pangenotypic drugs, so, baseline HCV genotyping is required.

With all of these efforts, we hope that HCV burden in Thailand will gradually reduce with simultaneous reduction in complication of chronic liver disease and hepatocellular carcinoma.
The most common hepatitis C virus (HCV) genotype is 1b, accounting for approximately 55%, followed by 2 (~44%). Currently available direct acting antiviral (DAA) ledipasvir/sofosbuvir for genotype 1, sofosbuvir + daclatasvir for genotype 1 and 3, daclatasvir + asunaprevir for genotype 1b, sofosbuvir + ribavirin for genotype 2 and 3. The regimen of elbasvir/grazoprevir for genotype 1 and 4, omitasvir/paritaprevir/ritonavir + dasabuvir for genotype 1 will be soon available in South Korea.

Firstly, daclatasvir plus asunaprevir (DCV+ASV) treatment has demonstrated potent antiviral activity in patients with genotype 1b hepatitis C virus (HCV) infection. In the real-world efficacy, changes in liver stiffness measurements and safety of DCV+ASV treatment in our institute. A total of 306 patients with chronic hepatitis C were treated with DCV+ASV from August 2015 to July 2016. We excluded patients with resistance-associated substitutions (RAS) in NS5A and hepatocellular carcinoma at baseline. The patients received DCV (60mg once daily) plus ASV (100mg twice daily) for 24 weeks. Finally, 212 patients who were followed up for 12 weeks after the end of treatment were analyzed. We investigated virologic response and the changes of fibrosis with non-invasive markers before and after completion of the treatment. The mean age was 60.8 years and female was predominant (63.2%). Treatment-naïve patients (61.8%) were in the majority and 44 (20.8%) patients had cirrhosis. 208 (98.1%) and 204 (96.2%) patients achieved end of treatment response and sustained virological response (SVR12), respectively. SVR12 rates were higher in patients who were less than 65 years old, male gender, those with cirrhosis and those with lower HCV RNA. Significant decline was observed in LS values, FIB-4 and APRI values between baseline and SVR12 regardless of presence of cirrhosis and treatment experience. In conclusion, DCV+ASV dual therapy resulted in high SVR12 rates with improved liver fibrosis and the treatment was well tolerated in patients with genotype 1b HCV infection. Further studies are needed to monitor the long-term results of the DCV+ASV treatment.

In this presentation, the efficacy and safety of various antiviral regimens using DAAs for genotype 1 and 2 in real-life setting will be discussed. Also, Korean strategy of HCV eradication will be introduced.
About 1.5-2 million Japanese people are infected with HCV. However, the prevalence of HCV in Japan especially among younger generations is decreasing because of the successful implementation of prophylaxis programs, such as HCV screening for blood transfusion and blood products, usage of disposable syringes for mass vaccination. Further Japanese Government support for Toshiba General screening HCV and HBV infected patients from 2002 and until 2006, almost all the people at the age of 40, 45, 50, 55, 60, 65, and 70 were checked for anti-HCV and HBsAg at annual medical checkups by local governments. More than 9 million residents have been screened and 100,000 hepatitis patients were detected at the checkup. Japanese parliament passed “Basic Act on Hepatitis Measures” on November 30th, 2009 for preventing and offering adequate treatment for viral hepatitis. Thus, all the HCV patients are treated with the latest treatment in reduced expense. HCV treatment dramatically improved in recent 2 decades, interferon monotherapy started 1991 with low SVR rate (2%). Then ribavirin appeared 2001 and SVR rate increased to 20%, pegylated interferon (2003) improved SVR rate to 50%. DAA (direct acting antivirals) were approved in 2012 in combination with interferon, and SVR rate increased up to 85%. Now interferon-free DAAs therapy are available and more than 95% patients can eliminate HCV in sera. Powerful anti-HCV drugs are available right now, however, new problems, HCC after HCV elimination, have come up. Thus, anti-HCV therapy in Japan is now concentrated on containment of progression of liver HCV-induced liver diseases, not merely HCV-free status of HCV-infected patients.
HCV genotype 4 (HCV-4) is the cause of approximately 15-20% of chronic hepatitis C in the world. In Egypt, GT4 accounts for approximately 90% of infections, with subtype 4a predominating. Egypt with its current population of close to 90 million has the highest HCV prevalence in the world; 14.7% of the Egyptian Liver Research adult population. Egypt has an estimated annual incidence of about 150,000 Institute and Hospital cases. HCV-related HCC currently tops the list of cancer-related mortality. (ELRIAH)

The strategic targets are: to decrease HCV prevalence to <2% in Egypt in <15 years (Mathematical modeling); Treating 200,000-300,000/year, by drugs with cure rate >90% and treatment prioritization to high risk people. Early in 2014, the Egyptian government represented by its Ministry of Health (MOH) and the National Committee for Control of Viral Hepatitis (NCCVH), successfully signed a memorandum of understanding (MoU) with Gilead; according to which, Gilead accepted to supply its DAA brand, Sofosbuvir at only 1% of its price in the USA. This price was close to 300USD/28 cap box. Fifty specialized governmental centers are sharing in the project Treatment in its first phase: included only cases with F2, F3 F4 or compensated cirrhosisi. Age limits for treatment legibility fixed to be above 18 years and below 70 years for all patients while BMI will be accepted up to 35. At the beginning of the project to protocols have been applied: IFN-based regimen: PeglFN alpha+Ribavirin (weight based; 1200 mg if ≥75 Kg or 1000 mg if < 75Kg of body weight)+ Sofosbuvir 400mg/d for 12 weeks; basically received by INF-eligible patients. IFN-ineligible patients:

- **Sofosbuvir 400mg/d+Ribavirin** (weight based; 1200 mg if ≥75 Kg or 1000 mg if < 75Kg of body weight) for 24 weeks.
- **NCCVH updated the treatment protocol:** (1) Treatment offered to all HCV PCR positive patients. (2) Adding Simprevir for non-INF-eligible patients:
  - **Sofosbuvir 400mg/d+Simprevir 150mg/d** for 12 weeks. (3) Later on: SOF/DAC and SOF/DAC/RBV were added.

Professor Shinpei Sato

Toshiyuki Kawai, Takafumi Sugimoto, Miho Kanda, Yuji Kondo.

Kyoundo Hospital, Liver Unit, Tokyo, Japan Friday, June 16, 2017 12:10-12:20
We introduced adjustable RFA electrode needle (VIVARF system) which became usable from 2015 in order to improve therapeutic results of radiofrequency ablation therapy (RFA). We compared the short term results and their effects compared with the non-adjustable cool-tip electrode needle (covidien).

Methods:
RFA using the VIVARF system was enforced in 125 patients with liver cancer in 180 cases until 2015-2016. Of these, 65 cases (30 cases of hepatocellular carcinoma, 40 cases of liver metastasis) enforced by February.

All cases were performed percutaneously. We compared 50 cases of nonadjustable cool-tip electrode needles used at the same time as adjustable RFA electrode needle. We analyzed the results of treatment, local recurrence and complications for liver cancer. The tumor diameter was 2.1 cm (1.0 - 7.0), and the average number was 1.5 (1 - 9).

Results:
The adjustable type had a larger tumor diameter (2.6 cm) and a significantly larger number of tumors (2.1). Tumor remnants by evaluation CT were both 0. Local recurrence was 4 cases (5.7%) in variable type, 3 cases (6%) in nonadjustable type (average observation period 9 months). Complications were skin burned in 3 cases (4.2%) adjustable type, 1 case (2%) in non-adjustable type. A cause of skin burn was due to damage to the coating of electrode needle by induction needle in adjustable type. The use of adjustable type was useful for 80% of cases, of which 55% was useful for the control of the ablation zone and 45% for multiple lesions.

Conclusion:
Adjustable RFA electrode needle was able to be safely carried out comparable to treatment effect compared with non-variable type cool-tip electrode needle. Multiple lesions were efficiently treatable.
KEYNOTE LECTURE I

Moderator
Professor Ming Lung Yu
Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Professor Pagbajav Nymadawa
Mongolian Academy of Sciences, “Gyals” Medical Center, LLC, Ulaanbaatar, Mongolia

Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
Friday, June 16, 2017 12:30-12:55

Professor

Lai Wei
Peking University
People’s Hospital,
Beijing, China
LS1-1: Clinical Importance of Preexisting Polymorphism

Because of lack of proof reading activity of HCV RNA-dependent-RNA polymerase (NS5B) and high replication activity of HCV, large number of viral variants are produced continuously during infection with an error rate $10^{-3}$ to $10^{-4}$ mutations per nucleotide per genome replication [R.Bartenschlager and V.Lohman, 2000].

Direct-acting antiviral agents (DAA) against HCV open a new era for antiHCV therapy but DAA resistance-associated variants (RAV) could jeopardize the effectiveness of DAA [WHO, 2016; T.Shin-I, M.Sugiyama, M.Mizokami, 2016]. RAV may be arise under pressure of DAAs, and also may naturally exist among the variants of HCV population.

The screening of GenBank data base for HCV sequences has revealed RAV in 58.7% (854/1455) sequences [Zhi-wei Chen, et al., 2016].

In this lecture, the frequencies of the most common RAVs and their clinical significance and the preventive measures against development of RAVs will be reviewed from the world literature.
Keynote lecture II

Professor Shiv Kumar Sarin
Hepatology and Director, Institute of Liver and Biliary Sciences, New Delhi, India

Professor Kwang-Hyub Han
Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea

Professor Khuyag Bayanmunkh
General surgeon, Liver and pancreatic surgeon, Santso surgery clinic
Sorafenib was the first oral molecular targeted agent to show a survival benefit in patients with HCC. Many trials have been conducted to develop new agents that can replace sorafenib as a more potent and safe first-line therapy. However, the superiority or non-inferiority of sunitinib, brivanib, and linifanib to sorafenib could not be proven.

Furthermore, clinical trials of brivanib, everolimus, ramucirumab, tivantinib were conducted with the aim of developing second-line agents for patients unresponsive to or intolerant of sorafenib, but failed to show superiority to the placebo. However, because ramucirumab was highly effective in a group of patients with elevated serum alpha-fetoprotein (AFP), a phase III study of ramucirumab is currently underway in patients with serum AFP levels ≥400 ng/ml.

Recently, positive results of lenvatinib and regorafenib for hepatocellular carcinoma (HCC) have been reported. They would be definitely the other standard of care agents.

An antibody against programmed cell death protein 1 (PD-1) has been gaining attention as an immune checkpoint inhibitor in recent years. At ASCO 2015, a phase I/II study of anti-PD-1 (nivolumab) in patients with HCC reported a favorable outcome, with two complete and seven partial responses and an overall response rate of 19%. The outcomes of the dose escalation and dose expansion trials were reported at ASCO 2016. Furthermore, other reports included the design of a phase III clinical trial including Nivolumab as first line setting and Pembrolizumab as second line setting. And a study of combination therapy with anti-PD-1 and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) is also ongoing.

In ESMO 2015, extremely good results of a combination therapy of pembrolizumab with lenvatinib have for the B types of solid tumors been reported. These combination therapies will be the future promising treatment agents for HCC.
Cirrhosis is the end result of almost all chronic diseases that afflict the liver. It has been clear since ancient times that it encompasses a spectrum from mild asymptomatic cases to severe endstage liver failure with a poor short-term prognosis [1]. The deterioration from mild to severe is often not gradual nor linear but occurs in ‘bursts’ or short periods of time, sometimes precipitated by an acute event such as sepsis.

I believe that the major factor to explain most decompensation is centred around cardiovascular ‘insufficiency’. Such insufficiency is composed of several sub-mechanisms[2-6]: 1) ischemia/hypoxia of the liver leads to increased fibrogenesis and parenchymal extinction. Extinction is a hypothesis developed over the past 25 years by Wanless to explain cirrhosis histological progression that results in apoptosis, atrophy, obliteration of liver cell mass and fibrogenesis. 2) Portal hypertension results in gut congestion/ischemia leading to increased bacterial translocation and an inflammatory phenotype. 3) Peripheral arterial vasodilation leads to decreased effective circulating volume [DECV]. 4) Venous insufficiency, manifested as a ‘sump’ effect and inability to mobilize the capacitance reservoirs of the circulation, contribute to the DECV. 5) Pump function (the heart) is inadequate, further worsening DECV. This condition is known as cirrhotic cardiomyopathy. 6) Anemia due to gastrointestinal bleeding or the chronic anemia of cirrhosis, also decreases the oxygen-carrying ability of the vessels. 7) The coagulopathy of cirrhosis results in microthrombi in the liver microcirculation, with perfusion mismatches and eventually the extinction cascade.

Many of these mechanisms are self-propagating positive feedback loops that can magnify the effects of small perturbations. For example, gut bacterial translocation is worsened by portal hypertension/gut ischemia, which sets up a systemic inflammatory phenotype that impairs cardiovascular responsiveness in the heart and vessels, which further worsens the gut ischemia.

I will present evidence for some of these mechanisms in various animal models of liver disease. Suggested management is offered, at this point based more on educated speculation rather than firm evidence.

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide and approximately 750,000 new cases are diagnosed each year.

There has been a marked increase in HCC-related annual death rates during the past two decades. At present, HCC represents a major public health problem in the Asia-Pacific region. Most patients with HCC are diagnosed at advanced stage. Although management of HCC has been remarkably improved since 20 century, unsolved issues are still remained and overall prognosis is still grave in advanced stage. Molecular targeted therapy opened new era and emerging immunotherapy is promising to overcome current barrier. However, it will be a long way to get excellent long-term outcome. In addition, cost burden can be a big huddle to manage HCC patients in developing Asian countries.

Fortunately, HCC is preventable disease and early diagnosis is the key factor to improve survival outcome. Therefore it is important to know risk factors and predict risk of HCC development.

Worldwide, approximately 80% of HCC is caused by hepatitis B virus (HBV) and/or hepatitis C virus (HCV) infection. In addition, the single largest risk factor in the development of HCC is cirrhosis of any etiology. The best way to control HCC is primary or 2ry prevention of HCC. Potent antiviral agents may reduce the risk of HCC development in the near future.

Friday, June 16, 2017 15:15-15:40

Chronic delta hepatitis (CDH) is the most severe form of chronic viral hepatitis. It develops as a result of HBV-HDV co-infection. HDV alone is able to replicate but needs the helper function from the hepatitis B virus (HBV) consisting of
hepatitis B surface antigen production to complete virion assembly. Only then, it is able to lead to propagate HDV infection to other hepatocytes and as a consequence causing liver disease in humans. HDV is today a disease of developing countries. It is infrequently observed in the industrialized world and has received the designation of orphan disease in the US and the European Union. In these parts of the world HDV is mostly observed in high risk populations such as intravenous drug users and in migrants from HDV endemic countries. CDH is an immune mediated disease and various host and viral factors may affect the course of the disease. Among viral factors HDV genotypes are important. Eight genotypes based on a sequence variation of 19 to 38% have been described for HDV. HDV I has a worldwide distribution. Genotype II HDV seen in the Far East is associated with a milder form of chronic hepatitis compared to genotype I. Genotype III HDV is observed in the Amazon region of South America and is associated with a particular severe clinical presentation. Genotype IV, reported formerly as genotype IIb, has been seen both in the Far East and Africa. Genotypes V to VIII, are seen exclusively in Africa. African CDH patients may be associated with a mild form of the disease and may respond better to interferon treatment. The striking developments in the last 15 years seen in chronic hepatitis B and chronic hepatitis C treatment have not been seen in CDH. Biomedical industry did display little interest in searching for new treatment options in CDH and the current management of proven benefit in CDH continues to be treatment with interferons. New strategies for finding a “functional cure” in HBV would be beneficial also for HDV patients. Meanwhile, new therapeutic strategies devoted to HDV only or tailoring both HBV and HDV have reached phase II studies in humans. These consist of the use of hepatocyte entry inhibitors, farnesyl transferase inhibitors and nucleic acid polymers. These approaches are tailored towards cellular attachment of HDV to the hepatocyte, virion assembly and viral extrusion from the hepatocyte, respectively. New treatments for CDH are an urgent need as liver-disease related complications continue to negatively effect the natural course of this disease.
Treatment Strategy of HCV Infection in Asia

Professor Cihan Yurdaydin
University of Ankara Medical School, Ankara, Turkey

Professor Khin Maung Win
Honorary Professor, Yangon, Myanmar

Professor Janchiv Oyunbileg
Leadingscientist, Public Health Institute, Mongolian Academy of Medical Sciences
Hepatitis C virus (HCV) infection remains one of the most important causes for the liver cirrhosis (LC), hepatocellular carcinoma (HCC) and liver-related mortality. Since successful HCV eradication, namely the achievement of a sustained virological response (SVR) with anti-viral therapy greatly reduces the incidence of HCC, it is considered the general recommendation that it is necessary to try the best to cure all patients with HCV infection (viremia). However, in the era of previous standard of care (pegylated interferon (PegIFN)/ribavirin combination therapy), the efficacy and safety of this treatment regimen are sub-optimal because of the relative higher rate of treatment failures and some problems of tolerance or eligibility. With the innovative use of interferon-free, direct antiviral agents (DAAs) regimens, the obstacles encountered before seems to be easily overcome except the economic barrier: the cost. Therefore, the current HCV guidelines by major societies recommend that treatment should be prioritized for patients at the greatest risk for disease complications.

The IFN-free, DAAs regimens are not yet easily and broadly available in Asian, due to the most important barrier of financial barriers, particularly for many low income countries. With a high frequency of IL28B favorable genotype in Asian patients with chronic hepatitis C (CHC), IFN-based therapy may still play a role for Asian patients. The prioritization of CHC patients for anti-HCV therapy regarding to the IFN-based regimen may remain unchanged, however, the increased frequency of the intolerance or ineligibility will be expected. For the new DAAs, the prioritization of CHC patients for anti-HCV therapy can be based on the factors associated with the risk of complication such as the age and the fibrosis stage. We have elucidated the risk of development of HCC in Taiwanese patients who are younger than 40 years old or without/ with stage-1 fibrosis is very low. Hence in the resource-restricted areas such as many Asian countries, the treatment can be considered to be deferred. To overcome the barriers in eradication of the HCV infection, there will be no need for prioritization in treatment of HCV infection ideally.
therapy. Almost all DAAs are manufactured in the region, including Epclusa (the

Friday, June 16, 2017 16:05-16:20
combination of Sofosbuvir and Velpatasvir) which is the latest combination to be approved by the FDA. These drugs are manufactured according to two pathways: through voluntary licensing agreements with Gilead and other global manufacturers, and through non-licensed processes. APIs manufactured under licensed agreements currently come mostly from India and Egypt, and that manufactured in a non-licensed manner comes from India, China, Bangladesh, Pakistan and a few other countries.

Despite the availability of large scale generic production, the Asia-Pacific region is still largely limited in official access to these cheap versions of treatment despite such a massive patient burden and overall poor economic conditions of most countries in the region. This has necessitated the formation of buyer’s clubs and other NGOs which facilitate the treatment of patients privately through direct importation. On the other hand countries where generic DAAs are freely available have been able to upscale HCV treatment significantly over the past 2-3 years. Egypt for example has already treated a million HCV patients last year using generic products.

Overall, treatment results from the use of generics mirror match those available from large registration studies. Additionally, bioequivalence data is available in many instances from manufacturers of non-licensed products particularly. No major safety signals have been detected so far, although the development of resistant variants remains a possibility. Therefore the use of generic DAAs, both licensed and non-licensed, have brought down the cost of treatment massively in a number of Asia-Pacific countries and enabled the cure of a large number of patients which would otherwise not be possible. It is time that the Asia-Pacific region embraces the large scale use of generic DAAs in order to comply with the WHO goal of HCV eradication by 2030. The more important step then follows, and that is to ensure the quality of the generic products so as to ensure that our patients are treated in the best possible and yet the cheapest way.
therapy, 48 weeks and 24 weeks of pegylated IFN (Peg-IFN) plus ribavirin
The interferon (IFN)-based treatment of chronic hepatitis C virus (HCV) infection has begun since 1986. The "standard-of-care" of IFN-based therapy for HCV genotype 1 (HCV-1) and 2 patients, respectively. Furthermore, introduction of response-guided therapy that 24 weeks for HCV-1 with lower baseline viral loads (LVL, HCV RNA < 400,000 IU/ml) and a rapid virologic response (RVR, undetectable HCV RNA at treatment W4) and to 16 weeks for HCV-2/3 with a RVR could provide equal efficacy to “standard-of-care (SOC)". Interleukin-28B genetic polymorphisms have been associated with treatment efficacy with IFN-based treatment for HCV-1 patients, and might be useful in guiding HCV1 therapy.

Since the first directly acting antivirals (DAA) approved in 2011, the progress of DAA in HCV treatment is moving from IFN (IFN)-containing regimens to IFN-free regimens in 2013, which are currently standard-of-care. The IFN-containing regimens are almost no more recommended currently, such as boceprevir, telaprevir, simeprevir, and daclatasvir plus PegIFN/RBV due to the AE of IFN and unsatisfied efficacy. Sofosbuvir plus PegIFN/RBV for 12 weeks is still recommended for difficult-to-cure, IFN-eligible population, such as HCV-3 treatment experienced cirrhotic patients.

IFN-free regimens: Sofosbuvir plus weight-based dose of RBV, the first IFN-free regimen, is effective for all HCV genotypes, but only is recommended for HCV-2 with 12-week regimen. 12-week sofosbuvir-based therapies, plus ledipasvir or simeprevir or daclatasvir, the SVR rates could reach >90% for HCV-1-4 patients. Instead, 24-week daclatasvir plus asunaprevir is only recommended for HCV-1b with SVR rates of 85%-90%. The SVR rate decreased to 40% if patients harboring NS5A L31 or Y93 resistance-associated variants. PrOD regimen (co-formulated paritaprevir/r [NS3/4A PI boosted by ritonavir]/Ombitasvir and Dasabuvir) plus RBV for 12 weeks achieved high SVR rates (90%-95%) for naïve/experienced, cirrhotic/non-cirrhotic HCV-1 patients. PrOD without RBV also achieved a SVR rate of > 98% for HCV-1b, whatever cirrhotic/non-cirrhotic. Elbasvir/grazoprevir has been effective in HCV-1/ 4 (>90%), except for HCV-1a with NS3 RAV (around 70%). More recently, “one size fits all” regimen, such as sofosbuvir/velpatasvir (2nd generation NS5A) was shown to be highly effective for all HCV genotypes, compensated and decompensated liver diseases. Nevertheless, there challenges remain in the era of DAA, such as DAA failed patients, RAV, TEV and long-term outcomes.

OS 3-3: Evolution of Anti-HCV therapy

The interferon (IFN)-based treatment of chronic hepatitis C virus (HCV) infection has begun since 1986. The “standard-of-care” of IFN-based therapy for HCV genotype 1 (HCV-1) and 85%-90% for HCV-2 patients, respectively. Furthermore, introduction of response-guided therapy that 24 weeks for HCV-1 with lower baseline viral loads (LVL, HCV RNA < 400,000 IU/ml) and a rapid virologic response (RVR, undetectable HCV RNA at treatment W4) and to 16 weeks for HCV-2/3 with a RVR could provide equal efficacy to “standard-of-care (SOC)”. Interleukin-28B genetic polymorphisms have been associated with treatment efficacy with IFN-based treatment for HCV-1 patients, and might be useful in guiding HCV1 therapy.

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Treatment Strategy of Co-Infection

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Hepatitis B virus (HBV)/hepatitis C virus (HCV) co-infection is not uncommon in highly endemic areas and among subjects with a high risk of parenteral infections because of the shared modes of transmission. In Asia-Pacific countries, HCV superinfection in patients with chronic HBV infection was the most common clinical features of co-infection. HBV/HCV co-infected patients have been reported to have more severe liver injury, including liver cirrhosis and hepatic decompensation, and have a higher incidence of hepatocellular carcinoma as compared with mono-infected patients.

To cure the both HBV and HCV infection is the main goal in patients with HBV/HCV co-infection. Previous studies demonstrated that for patients with dominant HCV infection and low level HBV viremia, previous standard of care (pegylated interferon (PegIFN)/ribavirin combination therapy) can achieve a comparable sustained virological response (SVR) rate as expected with HCV mono-infection. With the current newly developed interferon-free, direct antiviral agents (DAAs) regimens, the high clinical efficacy for CHC can be also expected due to the high SVR rate in patients with HCV mono-infection. For patients with both active HBV/HCV infection, combination of the PegIFN/ribavirin and oral nucleos(t)ide analogs for CHB is considered a reasonable strategy.

The management of HBV/HCV co-infection has the major task of surveillance of both viral-related liver diseases. With successful clearance of the HCV by PegIFN/ribavirin therapy, the cure of HBV infection (clearance of HBsAg) is achievable with the effects of medication on CHB in patients with dominant HCV infection. It deserves further clarification that the effect of the usage of DAAs for CHC on the CHB. Actually, reactivation of HBV DNA was observed after PegIFN/ribavirin treatment even in the patients with low level of HBV DNA before therapy. In the era of all-oral DAAs, the reactivation of the CHB including HCV DNA and liver enzymes are reported which makes further elucidating the treatment strategy of HBV/HCV co-infection mandatory.
cirrhosis (LC), end stage liver diseases (ESLD) and hepatocellular carcinoma

Friday, June 16, 2017 17:15-17:30
Hepatitis C virus (HCV) infection is one of the leading causes of liver (HCC). The disease progression of chronic HCV infection to ESLD and/or HCC ranges from 20 to 30 years, depending on age at infection, viral genotype and viral loads, coexisting of alcohol consumption or comorbidities (diabetes and obesity), coinfection with HIV or HBV, gender and host genetics. The ultimate goal of anti-HCV therapy is to prevent the disease progression and ESLD/HCC. Successful HCV eradication by means of achieving sustained virological response (SVR, defined as HCV RNA seronegativethroughout 6 months of post treatment follow-up period) with interferon (IFN)-based antiviral therapy significantly reduces the incidence of LC, HCC development and liver-related mortality, as well as the risk of mortality from extrahepatic hepatic manifestations, and the risk of HCC recurrence after curative therapy for HCV-related HCC.

However, the risk of progression to cirrhosis and HCC/ESLD remains even after achievement of an SVR, especially that an unexpected high risk of HCC occurrence or recurrence were observed among HCV patients after successful antiviral therapy with IFN-free directly acting antivirals (DAA) regimens. Preexisting liver cirrhosis and age are well recognized the most important risk factor associated with HCC occurrence in HCV patients with an SVR. However, a substantial number of non-cirrhotic patients with an SVR remain at risk of HCC development. The pre-antiviral predictors of HCC include high baseline gamma-glutamyltransferase (rGT) levels, older age, significant fibrosis and genetic variants and serum levels of MHC class I chain-related A (MICA), and SNP rs17047200, located within the intron of the toloid like 1 gene (TLL1). The post-treatment non-invasive predictors include, elevated alfa-fetoprotein (AFP) levels, APRI, Wisteria floribunda agglutinin positive Mac-2-binding protein (M2BPGi), alanine aminotransferase levels (ALT) and serial liver stiffness by fibroscan. The identification of the risk surrogate biomarkers would help facilitating the follow-up strategy in HCV patients who have received antiviral therapy either with or without HCV eradication.
There are more than 30 million HIV patients worldwide with approximately 3-7 million or even more co-infected with hepatitis C virus (HCV). It is very common since both viruses have shared common route of transmission especially in people who are using drug, men who have sex with man. HCV/HIV coinfection is the bad combination since HIV reduces immune response and promotes high rate of HCV replication as well as low rate of spontaneous HCV clearance. With highly effective antiretroviral therapy (ART) decades ago, HIV is now well controlled so that patients can live long enough to develop long-term complication of chronic hepatitis C which again usually occurs earlier than in HCV mono-infected patients. HCV is not only more progressive but will usually interferes with ART treatment since liver abnormality is also the most common side effects of ART and sometime it is difficult to differentiate between drug effect and HCV flare.

HCV cure is the ultimate goal for these patients but with interferon based treatment, sustained virological response (SVR) is much lower than HCV mono-infection even the treatment mostly introduced when CD4 count greater than 200-500 cell/m³. Overall SVR rate with peginterferon/ribavirin was just 27-40% where SVR in HCV genotype 1 was much less. Moreover, there was high rate of treatment drop out due to side effects of treatment as well as drug-drug interaction with ribavirin such as didanosine.

Introduction of the first generation protease inhibitor such as boceprevir, telaprevir together with peginterferon/ribavirin which even made treatment of HCV more complex in these population with more pill burden, more side effects and more drug-drug interaction so that none has been approve for treatment of HCV/HIV co-infection and considered this group of patients as special population.

With the development of first all oral regimen some 5 years ago, it had shown that these treatment regimens have closed the gap of treatment response since treatment SVR currently is not different between HCV/HIV co-infection and mono infection even in the patients that CD4 count was still low. However, there are some concern regarding drug-drug interaction, reinfection of HCV and cost of treatment.

In general, HCV treatment can be initiated once HIV is controlled in order to avoid ART adjustment, side effects during early phase of ART treatment. Regimen for treatment of HCV/HIV co-infection usually the same as mono infection. Only the dosage of some drug such as daclatasvir should be adjust if used together with efavirenz. There are some concern regarding drug compliance and re-infection, so treatment should be start with patients discussion regarding these issues as well as harm reduction process in order to reduce further infection.

In conclusion, in this DAAs era, treatment of HCV/HIV co-infection has been improved with similar SVR rate as compare HCV mono-infection and this population is no more “special population”.

OS 4-3: Treatment Strategy of HCV/HIV Co-Infection

Professor Tawesak Tanwandee
Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
Friday, June 16, 2017 17:30-17:45
Saturday, June 17, 2017

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Professor Yasuhito Tanaka
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Professor Batmunkh Munkhbat
Vice President for Research and Development, Mongolian National University of Medical Sciences

Professor Shinpei Sato, Toshiyuki Kawai, Takafumi Sugimoto, Miho Kanda, Yuji Kondo.
Kyouno Hospital, Liver Unit, Tokyo, Japan
OP-001: Serum Vitamin D level and BsmI A>G (rs1544410) polymorphism of VDR

Enkh-Amar. B1, Enkhbilguun. S1, Amarbayasgalan. Z1, Chimeddhamsuren. G1, Dahgwaendorj. Ya1, Chimidtseren. S1,2

1Mongolian National University of Medical Science, 2B

Chronic hepatitis C viral (HCV) infection is a major cause of liver fibrosis and hepatocellular carcinoma (HCC). Currently, association of VDR gene polymorphism such as BsmI A>G (rs1544410) and chronic HCV infection are received much attention, due to VDR gene polymorphisms might be affected regulatory activity of vitamin D and causing more susceptibility to chronic infection.

The aim of this study was to test the serum Vitamin D level and BsmI A>G (rs1544410) polymorphism of VDR gene in patients with chronic hepatitis C infection compared with healthy persons.

Randomaly selected 30 patients with chronic hepatitis C infection and matching sex and age 60 (1:2) healthy volunteers (as control) were involved in this cross-sectional study. Genomic DNA were extracted from blood and the gene polymorphisms were identified by PCR and restriction fragment length polymorphism analysis. Serum vitamin D levels were determined by quantities enzyme-linked immunosorbent assay (ELISA) according to the manufacturer’s instructions.

In the VDR gene, BsmI A>G rs1544410 polymorphism were occurred 60% on GG, 5.7% on AA and 33.3% on GA genotype in control group. The genotype frequency were similar to patient group. In our study, deficient, insufficient, sufficient level of vitamin D in the serum were defined 73.3%, 20% and 6.7% of patients, 85%, 13.3% and 1.7 of healthy group, respectively.

No significant differences were observed for allele and genotype frequencies of BsmI A>Grs1544410 polymorphism in VDR gene, serum vitamin D level between patients with HCV infection and healthy groups (p > 0.05).

Saturday, June 17, 2017 08:07-08:14

OP-002: Functional and morphological abnormality of liver among diabetic patients with viral hepatitis/ m2bpogi and elastography changes comparative

Altantuya. I1, Uranbaigal. E1, Erdenetsogt. D1, Bira. N1, Otgonbayar. R1, Davaadorj. D1, Badamjav. S1, Sainbileg. S1

1Mongolian National University of Medical Sciences

Diabetic patients with viral hepatitis havea high risk of having liver cirrhosis. Therefore, screening of fatty liver and liver fibrosis in diabetic patients is more important. The main diagnosing method of fatty liver and liver fibrosis
is liver biopsy and histology but so far, we are able to detect viral infection using viral marker and determine fibrosis stage of NAFLD in patients who has diabetes mellitus type 2. There is no research to reveal viral infection, fatty liver and liver fibrosis in diabetic patients in Mongolia, so far. So it is necessary to study revealing viral infection, fatty liver disease and to determine stages of fibrosis using M2BPGi to screen liver fibrosis in diabetic patients.

To indentify viral infection, viral hepatitis in patients with diabetes and to compare liver function and diabetes control for diabetic patients with liver disease.

**Objective:**

To identify viral infection, viral hepatitis in patients with diabetes and to compare liver function and diabetes control for diabetic patients with liver disease.

**Methods:**

We got permission of research from the patients by handwriting signature who diagnosed Diabetes mellitus in National University Hospital. Hematology, biochemistry test, coagulation, immunology test are evaluated in 117 patients in clinical laboratory of National university hospital. We are used FIBROSCAN TOUCH 502 elastography in Mungun guur hospital. FibroScan® is based on Vibration Controlled Transient Elastography (VCTETM) at 50Hz. Quantification of fibrosis/kPa/quantification of steatosis /dB/m/. We studied the liver biopsies of 10 consecutive patients in clinical pathology division of Bio medical school of MNUMS. Place paraffin infiltrated tissue in a mold with a small volume of liquid paraffin. Based Paints Hemtoksilin Eozin all cases (H & E) determined by contrast, forms a good examination of a light microscope, fabrication and PAS stain on glycogen accumulation cell cytoplasmic and nuclear levels.

**Results:**

There were 117 patients and by average of ages 51-52 aged patient. The following up study diabetic patients type 2 n=78, diabetic patients with HCV n=39 two groups. Diabetic patients group in biochemistry test total cholesterol 4.78±1.16; triglyceride 2.62±1.54; HbA1c 9.46±4.37; in immunology tests M2BPGi (COI) counted 2.24±2.19 and fibroscan’s fibrosis 7.38±2.37, steatosis 290.6±50.5. BMI 31.6±4.5. 6 case possessed so-called glycogen nuclei of hepatocytes, 6% had PAS-positive thickening of blood vessels in the portal tracts. Diabetic patients with HCV patients group in biochemistry test total cholesterol 4.4±1.09; triglyceride 2.01±1.08; HbA1c in immunology tests M2BPGi (COI) counted 3.23±1.58 and fibroscan’s fibrosis 11.8±7.4, steatosis 290.6±50.5. BMI 29.8±4.9. Liver biopsy had central vein fibrosis, and sinusoidal fibrosis.

Diabetic patients group in immunology tests M2BPGi (COI) counted 2.24±2.19 and fibroscan’s fibrosis 7.38±2.37, 6 case possessed so-called glycogen nuclei of hepatocytes, 6% had PAS-positive thickening of blood vessels in the portal tracts. In liver biopsy fibrosis F1-2. Diabetic patients with HCV patients group in immunology tests M2BPGi (COI) counted 3.23±1.58 and fibroscan’s fibrosis 11.8±7.4. Liver biopsy had central vein fibrosis, and sinusoidal fibrosis. By M2BPGi glycobiomarker, we found that diabetic patients with viral hepatitis have more liver fibrosis.

**Conclusions:**

Diabetic patients group in immunology tests M2BPGi (COI) counted 2.24±2.19 and fibroscan’s fibrosis 7.38±2.37, 6 case possessed so-called glycogen nuclei of hepatocytes, 6% had PAS-positive thickening of blood vessels in the portal tracts. In liver biopsy fibrosis F1-2. Diabetic patients with HCV patients group in immunology tests M2BPGi (COI) counted 3.23±1.58 and fibroscan’s fibrosis 11.8±7.4. Liver biopsy had central vein fibrosis, and sinusoidal fibrosis. By M2BPGi glycobiomarker, we found that diabetic patients with viral hepatitis have more liver fibrosis.

Saturday, June 17, 2017 08:14-08:21
Viral hepatitis is a serious public health problem affecting billions of people globally. Mongolia has been considered to be highly endemic for hepatitis B and C virus infections. However, there have been little new data regarding general in the country.

In this abstract we aimed to report seroprevalence of HCV and co-infection among the general population aged 10-64 years in Mongolia.

The current study is the baseline survey of a Nationwide Cancer Cohort Study. Population based national cross-sectional survey was conducted with multistage random cluster sampling. Population aged 10-64 years in Metropolitan area and 4 geographic regions were randomly selected. Laboratory tests for HBsAg, HbcAb, anti-HCV were conducted using HISCL 5000 analyzer by the kits from SYSMEX Corp.Japan.

Among study subjects 37.2% were from rural provinces and 39.2% were men. Prevalence of HBsAg, anti-HBc, anti-HBs, HBeAg, and anti-HBe-positivity were 10.6%, 46.3%, 42.1%, 6.1% and 40.1%, respectively among general population aged 10-64 years. HCV infection was observed in 9.9% and 0.8% were co-infected with HBV and HCV. While the anti-HCV prevalence was significantly higher among women (11.7% vs.7.4%, P = 0.0001), HBsAg prevalence was higher among men (14.2% vs.9.1%, P = 0.0001). Both the infection with HBV (P = 0.0001) and HCV (P = 0.0001) significantly increased with age group from 10-14 years to 60-64 years. For instance, prevalence of HCV infection increased from 0.7% among population aged 20-24 years to 4.0% among elderly people aged 60-64 years.

In urban and rural areas of Mongolia, 1 in 5 person is infected with HBV and/or HCV, that is significantly associated with age, sex, and residence. The new study results recommends better preventive measures against these infections among general population.

Saturday, June 17, 2017 08:21:08-28

Open label clinical pilot study - SLASH C Trial

P. Patrick Basu, MD, MRCP, AGAF, N. John, M. Zaman, E Shehi, MD, M. Aloysius MD, PhD, N. Shah, MD, R. Brown Jr, MD, MPH

Chronic Hepatitis C (CHC) is no longer a clinical challenge in the era of DAA’s. CHC and SCD (Sickle cell Disease) contribute added challenges (sickle cell hepatopathy, accelerated fibrosis from chronic anemia and persistent secondary iron overload, ongoing cellular hypoxia induced by shear stress). Severe anemia and sepsis with IFN induced bone marrow failure precluded therapy.

This study evaluates the safety, efficacy and eradication of hepatitis C in this sub-group population with SCD.
Patient Characteristics:

Age range: 42 – 64

Demographics: African American 23/24, Hispanic African 1/24

IV drug abuser: 3/24

Mean Viral load: 869 - 5,600k

Genotype: 1a (9/24), 1b (11/24), 1a/4c (1/24), 1a/1b (2/24), 1a/3c (1/24)

Metavir Staging: F0 (4/24), F1 (5/24), F2 (7/24), F3 (4/24), F4 (4/24)

Mean Platelet Count: 142

Hemoglobin: 9.2 gm/dl

Ferritin, mean: 531

Transferritin saturation: 26

TB/Indirect Bilirubin: 6/4

Mean Haptoglobin: 29

Mean Retic Count: 7

Methods:

24 patients were recruited from three sickle cell centers in NYC.

Inclusion criteria: CHC (Geno specific with variation, diagnosed between 1998-2014) with SCD in remission (with sickle cell history > 30 years)

IL28B: TT allele in 21/24 patients, while CT allele in 3/24

All patients were placed LDV 90 mg + SOF 400 mg a day; with food for 12 weeks

Exclusion: Decompensated Cirrhotics, HIV, HBV, Sepsis, brittle SCD with frequent flares, uncontrolled DM, cardiomyopathy, CHF NYHA class III-IV, CKD, chronic osteomyelitis, active IVDU, Daily alcohol > 30 grams, Deferoxamine for 12 weeks

Results:

By Day 30, 22 out of 24 patients attained undetectable viral load. SVR 12 achieved was 91.6%.

Population Viral Failure: 8.3% (2/24), Out of the 2 failure, one had genotype combination 1a/4c and other had genotype combination 1a/3c.

Retention at the end of the study was 100%

Side events:

Nausea - 9/24 (37.5%), Constipation 6/24 (25%), Diarrhea 2/24 (8.3%), Headache 6/24 (25%), Abdominal pain 3/24 (12.5%), Renal Colic 1/24 (4.2%), Insomnia 8/24 (33.3%), Anemia 2/24 (8.3%), Hyperbilirubinemia 4/24 (16.7%), Urinary tract infection 3/24 (12.5%)

Conclusion:

This study demonstrates that LDV and SOF combination in SCD patients with CHC is safe and well tolerated; with an SVR12 of 91.67% (22/24) with 8.3% (2/24) viral failure (in concomitant genotypes; 1a/4c and 1a/3c). The drugs were well tolerated with minimal side events.

Larger trials will validate further.
OP-005: Alpha-Fetoprotein Response after Selective Internal Radiation Therapy versus Sorafenib in locally advanced hepatocellular carcinoma (SIRveNIB)

Ariunaa.Kh1, Sanduijav.R2, Bolormaa.Ya1, Tuyatsetseg.A1

1Mongolian National University of Medical Sciences

Objective: Alpha-fetoprotein (AFP) is considered to be an indicator of tumor activity in hepatocellular carcinoma (HCC). We present a novel correlation of AFP response to radiologic response and overall survival (OS) in patients treated with Selective Internal Radiation Therapy (SIRT) and Sorafenib therapies.

Methods: Participants from a phase III multicenter randomized trial of SIRT versus Sorafenib in HCC were studied. Thirty five patients with HCC were treated with selective internal radiation therapy or Sorafenib at our institution. Thirty one patients with baseline AFP higher than 20ng/ml were studied for analysis. AFP response was defined as more than 50% decrease from baseline. Twenty six patients with follow-up imaging were studied for the AFP imaging correlation analysis. We studied the relationship between AFP response and treatment outcome in terms of radiologic response and overall survival.

Results: Of 39 patients, 31 patients (79.4%) with elevated serum AFP (>20ng/ml) and documented radiologic evaluation every 12 weeks. AFP response was seen in 3 (17.6%) of 17 and 6 (40%) of 15 of patients treated with Sorafenib and Selective internal radiation therapy, respectively (P=0.16). The hazard ratio in AFP nonresponders compared with responders was 1.12 (95% CI, 0.46-2.69). AFP responders had better survival than nonresponders (15 and 6.95 months, respectively; P< .79), and AFP response was strongly associated with survival (hazard ratio, 1.12; 95% CI, 0.46 to 2.69; P< 0.79). AFP response were frequently observed in patients with radiologically stable disease (SD) and tended to indentify a subgroup of SD patients with better survival.

Conclusion: The data presented support the use of AFP response seen after locoregional therapy as an ancillary method of assessing tumor response and survival, as well as an early objective screening tool for progression by imaging.

Saturday, June 17, 2017 08:35-08:45

Mamun Al Mahtab

Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
There is limited data about the prevalence of hepatitis C virus (HCV) in Bangladesh. Most of the studies are also carried out in limited population. Published literature puts the figures to anything between 0.2% and approximately 1% in the general population. The same applies for Bangladeshi immigrants to Europe, as studies have that the prevalence of HCV among Bangladeshi immigrants in Spain and UK is 0.09 and 0.6% respectively. The figures, as expected, are much higher among high-risk population, being as high as 24.8% among intravenous drug abusers. However, it is generally accepted that the prevalence HCV in this country is 0.84%. Principal risk factors for the transmission of HCV in Bangladesh have been identified as treatment from quacks, shaving and haircut in barber shops, body piercing, as well as vaccination against small pox, cholera, dental procedure, intravenous infusion, etc. There is a male predominance with males accounting for more than 70% HCV infections. More than 60% HCV-infected people in Bangladesh are between 30 and 50 years of age.

HCV is the second leading cause of chronic liver disease in Bangladesh, next only to hepatitis B virus, accounting for 30% cases of liver cirrhosis and 17% cases of HCC. The predominant GT of HCV in Bangladesh is GT 3 (50-89%), followed by GT 1 (8-29%). Until 2015, the mainstay of treatment of HCV in Bangladesh was double therapy consisting of pegylated interferon (Peg IFN) and ribavirin (RIBA), with a reported SVR of 80% in GT 3. However, things have changed dramatically since February 2015, with the introduction of local, generic sofosbuvir (SOF) in our markets. We now also have local generic daclatasvir (DAC), valpatasvir (VAL) and ladipasvir (LPV), in addition to generic Peg IFN and RIBA. This has opened a whole new spectrum of affordable treatment for HCV for Bangladeshi patients, which has been facilitated by a favorable government policy of withdrawal of tax and VAT on anti-HCV drugs. The cost of DAC in Bangladesh is less than USD 1.0, no wonder why we are seeing a sudden influx of health tourism in Bangladesh not only from the region but also from Europe and USA. Initial data from Bangladesh with local generic direct acting antivirals (DAAs) are showing promising results comparable with the published literature. The government has finalized a National Strategy for viral hepatitis, the implementation of which will begin soon.
Chairs
Professor Diana Alcantara-Payawal
Fatima University Medical Center, Manila, Philippines
Dr. Huyag Bayanmunkh
General surgeon, Liver and Pancreatic surgeon,
Santso Surgery Clinic
KL-3-1: Beyond and Cure of HCV

Professor

Masao Omata
Yamanashi Central and Kita Hospitals, University
School of Medicine, San Francisco, USA Saturday, June 17, 2017 09:25-09:50

The eventual goal of management of decompensated hepatitis C patients is to provide long-term survival. Liver transplantation plays an important part in the process. Direct-acting antivirals (DAAs) that can be used in patients with hepatic decompensation provide opportunities to stabilize the patient and improve survival. Some of these patients may improve enough to be removed from the waiting list altogether whereas others continue to progress to death.
from liver failure. Some patients end up in the so-called MELD purgatory where the MELD score does not progress to allow the transplantation to occur but the patient’s quality-of-life does not recover to a desired level.

An alternative scenario is for patient to undergo antiviral treatment after liver transplantation. Compared to prior options, the currently available regimens afford much higher sustained virological response. Patients with hepatitis C may be at some advantage in accessing donor organ pool because they are able to receive HCV positive organs. However, post transplant patients may present a challenge to the clinician because of drug interactions that can potentially change the immunosuppression level or make the antiviral drug less effective. Also in the presence of immunosuppression, viral clearance may occur less effectively in transplant recipients than in immunocompetent individuals.

The current AASLD guideline spells out treatment options for hepatitis C patients with hepatic decompensation. This involves sofosbuvir plus a NS5A agent with ribavirin for 12 weeks or in patients who have contraindications for ribavirin extending the treatment without ribavirin for 24 weeks. In patients with DAA failure, 24 week regimens with ribavirin are recommended.

On the population level, liver transplant waitlist registration for hepatitis C in the United States has shown a noticeable change in the recent past. The rate of HCV patients with hepatic decompensation registering on the waiting list has been decreasing gradually overtime but the rate of decrease accelerated since the antiviral drugs became available. A part of this trend is attributable to aging of the HCV patients with increasing comorbidities that may make them no longer suitable transplant candidates. On the other hand, waitlist registrations have had more consistent rise for patients with hepatocellular carcinoma. Here, the most recent era showed slight reduction following a steady growth for over a decade.

It is highly likely that a part of this trend is attributable to widespread use of antiviral drugs which has been shown to improve the liver function as measured by Child Pugh classification or the MELD score. There is also optimism that as it was seen with hepatitis B patients, cirrhosis may reverse in those patients as well. Emerging data indicate that there is improved waitlist mortality for patients with HCV in the direct acting antiviral era. Similarly, the incidence of waitlist deregistration has increased recently.

In summary, management decision in patients with hepatic decompensation is complex. Patients with early-stage decompensation who have concomitant hepatocellular carcinoma, it would make sense to treat HCV prior to transplantation. For a CTP B or C patient with low MELD (i.e., <20) or for a live donor recipient, DAA treatment prior to transplantation may be beneficial for long-term transplant free survival or even in case of continued worsening, prevention of HCV recurrence. Patients who have a high MELD score and impaired renal function, proceeding with transplantation would be logical with a plan to treat post-transplant. Patients who are in between with moderate MELD score and preserved renal function, antiviral treatment should be individualized based on the patient’s symptoms, organ availability and comorbidities.
AASLD Guideline

Treatment for HCV in Patients with Hepatic Decompensation

<table>
<thead>
<tr>
<th>Genotype</th>
<th>RBV OK</th>
<th>No RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>SOF+VEL RBV (W) x 12 wk</td>
<td>SOF+VEL x 24 wk</td>
</tr>
<tr>
<td>1,4,5,6</td>
<td>SOF+LED RBV (L) x 12 wk</td>
<td>SOF+LED x 24 wk</td>
</tr>
<tr>
<td>1-4</td>
<td>SOF+DAC RBV (L) x 12 wk</td>
<td>SOF+DAC x 24 wk</td>
</tr>
</tbody>
</table>

Prior DAA failure: SOF+VEL=RBV or SOF+LED+RBV x 24 wk

RBV Dosing:
W (weight-based): 1200mg (Bwt<75kg), 1000mg (Bwt≥75kg)
L (low dose): 800mg
6th HCV conference
APASL Single Topic Conference 2017
16 - 18 June • Ulaanbaatar • Mongolia

APASL - WHO Joint Session

Chairs

Professor Masao Omata
Yamanashi Central and Kita Hospitals, University of Tokyo, Tokyo, Japan

Scientific Committee Chairman

Ying-Ru Lo, MD
Coordinator, HIV, Hepatitis & STI, Division of Communicable Diseases, World Health Organization, Regional Office for the Western Pacific Region
W1: An extraordinary response to prevent and treat chronic hepatitis B and C in the Western Pacific

Globally, 325 million people are living with chronic hepatitis. Of these, 129 million (40%) are living in the Western Pacific Region* (115 million with hepatitis B infection and 14 million with hepatitis C infection). The Western Pacific accounts for 40% out of 1.34 million deaths worldwide from hepatitis. Liver cirrhosis and cancer combined are the leading cause of deaths in the Western Pacific Region among 30-49 years old. We have now the tools to prevent these deaths. The WHO called upon Member States to adopt the regional action plan for viral hepatitis 2016-2020. This plan outlines a comprehensive response to viral hepatitis aiming at reducing incidence and mortality from viral hepatitis. Milestones and targets by 2020 include the reduction of prevalence of chronic hepatitis B to <1% in 5-year old children by 2017; development of national policies for health care worker hepatitis B immunization, and states ambitious hepatitis B virus (HBV) and hepatitis B virus (HCV) treatment targets aiming at 30% of estimated population living with HBV and HCV being diagnosed, 50% of the eligible population for treatment starting or being on treatment and 90% being virally suppressed.

The Region as a whole has made tremendous progress. Immunization programmes have reduced the regional prevalence of chronic hepatitis B infection to 0.9% among children born in the Western Pacific Region in 2012, meaning that the regional control goal of prevalence of chronic HBV infection <1% among 5 year-old children has been achieved. Harnessing universal HIV and syphilis screening programmes and interventions to prevent mother-to-child transmission infections are underway that will link HBV immunization to efforts to eliminate perinatal transmission of HIV and syphilis. As of 2015, 20 (including 9 Pacific Island Countries (PICs)/areas and 11 non-PICs/areas) out of 37 (54%) countries and areas in the Western Pacific indicated they had HBV health care worker vaccination policies. Hepatitis B and C treatment guidelines are known to be available in eleven countries. Countries regulatory authorities have received applications to register or have registered new hepatitis C medicines, and WHO recommended hepatitis B medicines are off patent in most countries. Several member states have introduced some form of reimbursement through national health insurance programmes for hepatitis B and/or C treatment.

* The Western Pacific Region of WHO covers 37 countries and areas such as Australia, China, Japan, Mongolia, Republic of Korea and the Pacific Island countries. For more information please visit http://www.wpro.who.int/countries/en/.
The Asian Pacific Association for the Study of the Liver (APASL) convened an international working party on APASL consensus statements and recommendations for management of hepatitis C in March 2015, to revise the APASL consensus statements and management algorithms for hepatitis C virus infection (Hepatol Int 6:409-435, 2012). The working party consisted of expert hepatologists from the Asian-Pacific region gathered at the Istanbul Congress Center, Istanbul, Turkey on 13 March 2015. New data were presented, discussed, and debated during the course of drafting a revision. Participants of the consensus meeting assessed the quality of the cited studies. The finalized recommendations for hepatitis C prevention, epidemiology, and laboratory testing will be presented.
Hepatitis C virus (HCV) infection is a major burden globally with wide regional diversity. Hepatitis C accounts for about 700,000 deaths per year, mainly from cirrhosis or hepatocellular carcinoma. In 2015, 71 million persons were estimated to be living with HCV viraemic infection. Hepatitis C treatment has been revolutionised with the advent of the direct acting antivirals oral drugs which cure infection after 12 weeks of treatment. The World Health Organization (WHO) launched the first Global Health Sector Strategy on Hepatitis 2016–2021 which outlines a set of global targets and priority actions for countries towards elimination as a public health threat by 2030. However, the focus of the strategy has been on the adult population, which bears the greatest burden of morbidity and mortality due to chronic liver disease. There is less discussions among clinicians, program and policy makers on the burden of HCV among infants, children and adolescents, and their inclusion in country and global response.

Challenges include major gaps in data, understanding of epidemiology and transmission, as well as evidence to inform how to manage pregnant women infected with HCV, infants, children and adolescents. Modelling studies in 2015 estimate 13.2 million children under 15 years of age with HCV antibody, while 6.6 million have viraemic infections. About 85% of children live in low and middle income countries. Transmission routes vary – mother to child transmission (MTCT) is the main route in developed countries, while in low and middle income countries, parenteral (unsafe injections, unsafe blood and blood products) and MTCT are commonly quoted main routes. Among adolescents, injecting drugs use is a risk. The landscape of treatment is changing with active research on use of DAAs to cure infection among children and adolescents. Most recently, the sofosbuvir-ledipasvir and sofosbuvir have been approved for treatment of HCV among adolescents without cirrhosis or with compensated cirrhosis, 12 years of age and older, or weighing at least 35kg.
An estimated 257 million people are living with hepatitis B virus infection (defined as hepatitis B surface antigen positive). In 2015, hepatitis B resulted in 887,000 deaths, mostly from complications (including cirrhosis and
hepatocellular carcinoma). Hepatitis B prevalence is highest in the WHO Western Pacific Region and the WHO African Region, where 6.2% and 6.1% respectively of the adult population is infected. In the WHO Eastern Mediterranean Region, the WHO South-East Asia Region and the WHO European Region, an estimated 3.3%, 2.0% and 1.6% of the general population is infected, respectively. The APASL HBV guidelines was revised which incorporated existing data to clinical practice guidelines based on evidence from existing publications or, if evidence was unavailable, on the experts’ personal experience and opinion after deliberations.

Universal HBV vaccination in newborns has dramatically changed the epidemiology of chronic HBV infection. A systematic review published by WHO experts in 2012 showed a decrease in prevalence of chronic HBV infection from 1990 to 2005 in most regions of the world.

Initial evaluation of an individual with HBV infection should include a detailed history and physical examination. A complete blood count, biochemical tests, serological and virological markers of HBV, and hepatic ultrasound should be part of the initial evaluation. The biochemical tests include ALT, AST, GGT, alkaline phosphatase, serum albumin and prothrombin time. The virological assessment consists of HBeAg, anti-HBe antibodies and Hepatitis B DNA measurement, the latter being the best marker of viral replication A real time PCR quantification assay should be used to measure serum HBV DNA levels. APASL guidelines reaffirms that there is still an important role for liver biopsy among chronic HBV infection, however, there is an apparent need to develop and use noninvasive, accurate, and reproducible tests for detecting liver injury. The utilization of noninvasive tests for assessing liver histology can significantly reduce, but not completely replace, the need for liver biopsy and should be seen as a complementary tool in the management of chronic HBV-infected patients. This seems to be an acceptable option in the real world in Asia.

Recommendations (results of currently available therapies, predictors of response to therapy, follow up and stopping rules during NA therapy in patients with chronic HBV infection)

- Treatment-naive patients can be treated with TDF 300 mg daily (A1), ETV 0.5 mg daily (A1), ADV 10 mg daily (A2), LdT600 mg daily (A2) or LAM 100 mg daily(A2).
- TDF or ETV are the preferred NAs and should be used as first-line
therapy (A1).

- During NA therapy, HBeAg, anti-HBe (inpatients with HBeAg-positive) and ALTs should be monitored every 3 months (A1). The HBV DNA level should be measured at month 3 and 6 of therapy and then every 3–6 months if agents with a low genetic barrier are used (lamivudine, adefovir, telbivudine), and every 6 months in patients treated with a high genetic barrier to resistance, such as entecavir or tenofovir (A1).

- Renal function and bone profile should be monitored at least every 3 months if TDF or ADV is used (A1).

- Muscle symptoms and muscle weakness should be monitored during telbivudine or clevudine therapy (A1).

- For HBeAg-positive patients without liver cirrhosis, the optimal duration of NA therapy is unknown, and the therapy can be stopped after at least 1 year (A1), but preferably after 3 years (C1) of additional therapy after HBeAg seroconversion with undetectable HBV DNA by PCR and persistently normal ALT levels.

- The optimal duration of NA therapy is unknown in patients with HBeAg-negative CHB. In patients without liver cirrhosis, the treatment can be withdrawn (1) after HBsAg loss following either anti-HBs seroconversion or at least 12 months of a post-HBsAg clearance consolidation period (B1), or (2) after treatment for at least 2 years with undetectable HBV DNA documented on three separate occasions, 6 months apart (B1).

- After stopping of NAs, patients should be monitored monthly for the initial 3 months and then every 3–6 months thereafter for relapse (A2).

Recommendations: results of currently available therapies, predictors of response to therapy, followup and stopping rules during interferon therapy in chronic HBV infection:

- Treatment-naive patients can be treated with Peg-IFN-a2a 180 ug weekly or Peg-IFN-a2b ug/kg weekly (A1).

- For Peg-IFN, the recommended duration is 48 weeks for both HBeAg-positive and negative patients (A1).

- In patients treated with Peg-IFN, full blood counts and serum ALT levels should be monitored monthly and TSH should be monitored every 3 months. All patients should be monitored for safety through 12 months of treatment (A1).

- In regions endemic for HBV genotype A and D infection, HBV genotyping should be done among patients being considered for IFN therapy (A1).
In HBeAg-positive patients, HBeAg and anti-HBe antibodies and serum HBV DNA levels should be checked at 6 and 12 months of treatment and at 6 and 12 months posttreatment (A1). HBsAg levels should be checked every 3 months (A1).

For HBeAg-positive patients treated with Peg-IFN who fail to achieve serum HBsAg levels below 20,000 IU/ml (genotype B and C infection), or any decline in serum HBsAg levels (genotype A and D infection) by week 12 and serum HBsAg levels below 20,000 IU/ml by week 24 (genotype A–D infection), stopping Peg-IFN therapy should be considered (B2).

In HBeAg-negative patients, serum HBV DNA levels should be measured at 6 and 12 months of treatment and at 6 and 12 months post-treatment (A1). HBsAg levels should be checked every 3 months (A1).

For HBeAg-negative patients, especially those with genotype D infection, who fail to achieve any decline in serum HBsAg levels and a [2 log10 IU/ml decline in serum HBV DNA levels by month 3 of Peg-IFN therapy, discontinuation of Peg-IFN therapy should be considered (B2).

There is the need for novel therapies—antiviral agents with new targets in the HBV replication cycle along with immunotherapies which are aimed at restoring the host immune response to HBV. The persistence of cccDNA in HBV-infected cells remains one of the main obstacles to complete eradication of the virus during chronic infection.
Professor W. Ray Kim  
Stanford University School of Medicine, San Francisco, USA

Professor Pagbajab Nymadawa  
Mongolian Academy of Sciences, "Gyals" Medical Center, LLC, Ulaanbaatar, Mongolia

Professor Osamu Yokosuka  
JCHO Funabashi Central Hospital/ Chiba University, Chiba, Japan
Professor Man-Fung Yuen  
Department of Medicine, LKS Faculty of Medicine, the University of Hong Kong, Hong Kong, China  
Saturday, June 17, 2017  
11:30-11:50

OS 5 - 1: Clinical Application of HBV Markers

Measurements of hepatitis B virus (HBV) markers in serum provide a convenient way to assess HBV disease activity which may be correlative to patient outcome. Measurement are usually done in qualitative and quantitative manners with the latter being more reflective and informative for the disease. Conventional measurements include qualitative HBsAg, HBeAg, anti-HBe and quantitative HBV DNA. Their roles are well characterized in many studies of disease natural history and of treatment. More recently, quantitative measurement of HBsAg levels become more attentive in HBV study field. A study showed that in HBeAg-positive patients, a higher HBsAg level is associated with a lower degree of fibrotic activity in the liver. And HBsAg levels remain static for many years after HBeAg clearance. It would only start to decrease after patients achieving status of undetectable HBV DNA. Achievement of HBsAg seroclearance in early age is of paramount important as far as the chance of development of long-term complications of HBV disease is concerned. Patients with HBsAg levels lower than 200 IU/mL would have a greater chance of achieving HBsAg seroclearance subsequently. While nucleos(t)ide analogs (NA) can achieve a high rate of HBV DNA undetectability, its reductive effect on HBsAg levels is negligible.

Recently, the roles of two novel serum markers namely hepatitis B core-associated antigen (HBcrAg) and HBV RNA are being actively examined in the scene of HBV. According to several studies, HBcrAg levels have associations with the following conditions: intrahepatic cccDNA levels, risk of development of hepatocellular carcinoma, chance of HBV reactivation after cessation of antiviral therapy in chronic hepatitis B patients; and chance of HBV reactivation in occult hepatitis B patients receiving immunosuppressive therapy. Studies on HBV RNA measurement are actively underway. Initial studies reveal that HBV RNA levels correlate with cccDNA levels and are associated with the risk of viral rebound after cessation of NA treatment.
OS 5-2: Treatment of Hepatitis B in Asia-Pacific

Hepatitis B is one of the major human diseases and estimated 400 million people are infected with HBV and cause approximately 800,000 deaths annually mainly by cirrhosis and hepatocellular carcinoma. Hepatitis B is dominantly seen in Asia-Pacific and in Africa, especially in East Asia. Various genotypes including genotype B, C, D are detected in Asia-Pacific. Recently, the number of infected persons is decreasing in young generation mainly by the protection with vaccination.

Various Nucleic acid drugs (NUCs) including telbivudine, adefovir, entecavir, tenofovirdisoproxilfumarate (TDF), tenofovirafenamide (TAF) are used for the treatment of HBV. Although these NUC treatment is effective for decrease of serum HBV DNA, ALT, and AST levels, they were not so effective for the decrease of HBsAg and long term use of NUCs is necessary. The cost for the treatment is a heavy economic burden for the people of Asia-Pacific countries.

IFN based therapy is also used for the treatment of HBV, however, the effect is limited and side effects are common, although treatment duration is finite usually for 24-48 weeks. The loss of HBsAg is more expected than NUC treatment, but the rate of HBsAg loss is not so high. Sequential therapy of IFN after NUC therapy is on clinical trial. Recently, combination therapy of TDF and Peg-IFN was reported to have better effect on HBsAg loss.

As these NUCs and IFN based therapy seem to be not enough, new compounds are exploited recently. Based on the replication pathway of HBV, clinical trials are undergoing on various drugs such as HBV entry inhibitor (Myrcludex B), RNAi (ARC-520), HBV core assembly inhibitor (GLS4), etc.

OS 5-3: Clinical Significance of Occult HBV Infection

The possible pathogenic role of occult hepatitis B infection (OBI) were studied in many studies. Most of the OBI patients have normal liver enzymes and minimal or no liver necroinflammation and fibrosis. HBV usually replicates at a low level inside the liver. However, OBI may still be associated with the development of liver cirrhosis and hepatocellular carcinoma (HCC). OBI as the etiology for development of cirrhosis and HCC has been well reported in the setting of co-infection with chronic hepatitis C infection. The estimated frequency of OBI in patients with cryptogenic liver cirrhosis ranges from 4.8 – 40%.
As early as 1985, a study had reported that HBV DNA was detectable in the liver of HBsAg-negative patients with HCC. Subsequent studies found that 45–80% of patients with apparently unidentifiable cause of HCC were having the HBV detected in the liver. These data suggest that OBI is associated with the occurrence of HCC. A longitudinal follow-up study conducted in Japan confirmed OBI would increase the risk of HCC.

Another important area of OBI is HBV reactivation. HBV reactivation rate ranges from 9% to 24% in several retrospective studies. According to a most recent prospective study, 40% of HBsAg-negative and anti-HBc-positive patients receiving rituximab developed HBV reactivation. Anti-HBs-positive subjects although still had a considerable rate of HBV reactivation (34.4%), it was significantly lower than that of anti-HBs-negative subjects (68.3%, p=0.012). HBsAg-negative and anti-HBc-positive patients receiving haematopoietic stem cell transplantation also have the HBV reactivation rate of 40%.

In summary, OBI plays an important pathological role in different aspects of chronic liver disease. Vigilant investigations and monitoring of the disease flares and complications are required in specific groups of patients.

Professor Yasuhito Tanaka
Department of Virology & Liver Unit, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Saturday, June 17, 2017 12:30-12:50
The risk of developing hepatocellular carcinoma (HCC) is not completely abrogated after eradication of hepatitis C virus (HCV) by anti-viral agents. We aimed to identify host genetic variation associated with the development of HCC after achieving sustained virological response (SVR) in chronic hepatitis C (CHC) patients.

Methods: We conducted a genome-wide association study (GWAS) in 456 Japanese patients who achieved SVR by interferon-based therapy, followed by a replication analysis of 79 candidate single nucleotide polymorphisms (SNPs) in an independent set of 486 patients.

Results: SNP rs17047200, located within the intron of TLL1 on chromosome 4, showed a strong association with developing HCC at a genome-wide level of significance when the results of the GWAS and the replication cohort were combined (odds ratio = 2.37, \( P = 2.66 \times 10^{-8} \)). Multivariate analysis showed that rs17047200 AT/TT was an independent risk factor for developing HCC (hazard ratio = 1.78, \( P = 0.008 \)) in addition to other factors. Combining the rs17047200 genotype with other factors, we propose different prediction models for HCC development in patients with mild or advanced hepatic fibrosis. TLL1 expression analyses showed that mRNA levels in human stellate cells increased with activation. Moreover, Tll1/TLL1 mRNA increased in liver tissues of rodents with hepatic fibrogenesis and CHC patients with progression of hepatic fibrosis. Gene expression levels of TLL1 short variants, including isoform 2, were higher in patients with rs17047200 AT/TT.

Conclusion: We suggest that genetic testing for the TLL1 SNP might be used to identify patients at risk for HCC after an SVR to treatment of HCV infection.
## LUNCHEON SYMPOSIUM II

13:00-14:00 Supported by Sysmex Corporation

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<tr>
<th>Time</th>
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<th>Chair(s)</th>
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<td>Opening speech</td>
<td>Hisashi Narimatsu</td>
<td>Tokyo</td>
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<tr>
<td>13:30-13:50</td>
<td>HBV and HCV infections in different social groups in Ulaanbaatar, Mongolia</td>
<td>Tsendsuren Oyunsuren</td>
<td>Ulaanbaatar</td>
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<td>13:00-14:00a0</td>
<td>Discussion</td>
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Chair
Education
Year of graduation Degree Affiliation
1974 MD Keio University School of Medicine, Japan
1979 PhD Keio University Graduate School of Medicine, Japan

Professional Experience

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<th>yyyy.mm</th>
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<tbody>
<tr>
<td>1979/4-1983/3</td>
<td>Instructor Department of Microbiology, Keio University School of Medicine</td>
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<tr>
<td>1983/4-1985/4</td>
<td>Postdoctoral Fellow Laboratory of Immunology, National Institute of Allergy and Infectious Disease (NIAID), National Institutes of Health (NIH), Bethesda, Maryland, USA</td>
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<tr>
<td>1985/5-1986/3</td>
<td>Postdoctoral Fellow Laboratory of Pathophysiology, National Cancer Institute (NCI), NIH with Dr. Pradman Qasba, USA</td>
</tr>
<tr>
<td>1986/4-1986/9</td>
<td>Instructor Department of Microbiology, Keio University School of Medicine</td>
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<tr>
<td>1986/10-1991/3</td>
<td>Associate Professor Instructor, Department of Microbiology, Keio University School of Medicine</td>
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<tr>
<td>1991/4-2000/9</td>
<td>Professor Division of Cell Biology, Institute of Life Science, Soka University</td>
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<tr>
<td>2000/10-2002/5</td>
<td>Principal Research Scientist Group Leader of Gene Function Analysis, Institute of Molecular and Cell Biology, National Institute of Advanced Industrial Science and Technology (AIST)</td>
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<tr>
<td>2002/6-2006/12</td>
<td>Deputy Director Research Center for Glycoscience, AIST</td>
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<tr>
<td>2002/6 to present</td>
<td>Professor Graduate School of Comprehensive Human Sciences, Tsukuba University</td>
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<tr>
<td>2006/8 to present</td>
<td>Coordinated Member Science Council of Japan</td>
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<td>2006/12-2014/3</td>
<td>Director Research Center for Medical Glycoscience, AIST</td>
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<tr>
<td>2011/4 to present</td>
<td>Visiting Professor Keio University School of Medicine</td>
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<tr>
<td>2011/7 to present</td>
<td>Advisory Professor Shanghai Jiao Tong University, China</td>
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<td>2014/4 to present</td>
<td>Invited Senior Researcher</td>
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<tr>
<td>2011/4 to present</td>
<td>Researcher Emeritus Biotechnology Research Institute for Drug Discovery, AIST</td>
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Academic Society (Current) position

| Society |
| Council member Human Proteome Organization |
| Steering committee member Asian Community of Glycoscience and Glycotechnology |
| Councilor Japanese Society of Carbohydrate Research, |
| Permanent council member Japan Consortium for Glycobiology and Glycotechnology |
| Councilor Japanese Biochemical Society |
| Councilor Japan Society for Molecular Tumor Marker Research |
| Member Science Council of Japan |

Council member Japanese Proteomics Society
Member Japanese Cancer Association
2010/5 Chemistry-Bio Tsukuba Award: Tsukuba Foundation for Chemical and Biotechnology
2011/7 Tsukuba Award: Science and Technology Promotion Foundation of Ibaraki
2013/9 JHUPO Award: Japanese Proteomics Society
2015/4 President Award: National Institute of Advanced Industrial Science and Technology (AIST)
Introduction: Hepatitis C and Hepatitis B virus establishes persistent infection that often results in chronic hepatitis followed by liver fibrosis, cirrhosis, from which hepatocellular carcinoma arises. Mac-2 Binding Protein Glycosylation isomer (M2BPGi) is a new serological glyco-biomarker that has been recently developed for predicting the stage of liver fibrosis. We aimed to determine M2BPGi marker among HBV and HCV infected and non-infected general population aged 10-64 years in Mongolia.

Methods:
A nationwide population based cross-sectional study was conducted with multistage random cluster sampling. Laboratory analyses for M2BPGi, AFP, HBsAg, Anti-HBs, HBeAg, Anti-HBe, Anti-HBc, Anti-HCV were performed using HISCL-5000 analyzer and kits of SYSMEX Corporation, Japan. Data collection was conducted between September 2016 and February 2017.

Results:
A total of 6674 people were enrolled from 8 provinces and capital city. Among general population, aged 10-64 years 34.9% had increased level of M2BPGi, that was observed in 30.2% and 38.2% among men and women, respectively (p<0.01). According to study areas, high level of M2BPGi was found in 40.2%, 32.5% and 29.6% in capital Ulaanbaatar, province centers and rural soums, respectively. In addition, it was significantly increased by age increase. Subjects infected with HBV and HCV had significantly higher rate of M2BPGi compared to apparently healthy subjects. For instance, increased level of M2BPGi was found in 74.4% among HBV and HCV co-infected and in 73.3% among HCV-infected subjects, whereas it was significantly decreased to 37.4% among healthy participants (p<0.001). Mean M2BPGi concentration was 1.70±0.16, 1.66±0.07, and 0.9±0.03 in the above groups, respectively (p<0.0001).

Conclusion:
High level of M2BPGi, a new biomarker of liver fibrosis was observed in 34.9% of general population aged 10-64 years. The levels of M2BPGi was significantly different by HBV and HCV infection status as well as by sex, age, and urban rural residence.
In Mongolia, since 1992 when our group of researchers started to analyze HBV and HCV infection in inhabitants of Ulaanbaatar city, its distribution has been changed due to an improvement in diagnostics, human life styles, medical services and others in last years.

In order to develop current policies and strategies for combating viral hepatitis in Mongolia it is imperative to describe the present situation of hepatitis infections, especially in Ulaanbaatar city where about a half of country’s population is situated nowadays.

The present study was conducted in randomly selected social groups in Ulaanbaatar, which included factory workers, university students and scientific researchers. In total 835 subjects were enrolled in the study, including 198 factory workers, 182 university students and 455 researchers from age 20 to 79 years. From all screened adults 410 (49.1%) were men and 425 (50.9%) were women. In first 2 groups blood serum samples were tested for HBsAg and anti-HCV by ELISA method. For examination of the third group the chemiluminescent enzyme immunoassay (CLEIA) based a fully automated immunoanalyser HISCL-800, Sysmex Corporation, Japan was used.

In results the overall prevalence of HBsAg and anti-HCV among studied subjects were 11.6% (97) and 13.9 % (116), respectively. 2.1% was positive for both virus markers and there was not significant gender differences. In third group of subjects 11.2% and 15.6% was positive for HBsAg and anti-HCV respectively. 1.3% (6) was positive for both markers. In HBV cases, HBsAb, HBcAb, HBeAb and HBeAg as well as HBcAb were tested. In results, while titer of marker proteins were ranging from < 0.2 IU/ml to 2500 IU/ml and more, positivity for HBsAb, HBcAb, HBeAg, HBeAb were 86.6%, 57.8%, 2% and 51.9% respectively.

Positive rate of anti-HCV was increasing by age from 5.4%, 16.5% and to 25.4% in <35 years to 36-50 and >51 years old groups. In anti-HCV positive subjects G1 was detected in 61%, G2 in 15% and in remaining samples serotype was not detected.

From these results it was concluded that HBV and HCV infection rate is still high in Ulaanbaatar with its slight shift of decrease in younger population.
New DA A Treatment and Liver Cirrhosis

Chairs

Professor W. Ray Kim  
Stanford University School of Medicine, San Francisco, USA

Professor Baatarkhuu Oidov  
Department of Infectious Diseases, Mongolian National University of Medical Sciences

Professor Samuel S. Lee  
University of Calgary, Calgary, Canada
Fibrogenesis of the liver is a response to injury. Hepatic stellate cells have a number of properties as a part of the cascade for inflammatory signaling, including proliferation, contractility, fibrogenesis, matrix deposition and chemotaxis. Emerging data indicate that fibrosis progression is a net result of fibrogenesis and fibrolysis.

The gold standard for assessing hepatic fibrosis has been the histological. As the liver undergoes fibrosis, not only is there fibrous tissue deposition but also parenchymal extinction which leads to formation of septum and adhesions. With the advent of effective antiviral treatment, there is increasing evidence of fibrosis regression, including in patients with cirrhosis. The recent proliferation of tools for noninvasive assessment the fibrosis has revealed there is a wide spectrum of pathology among patients with cirrhosis.

The prognosis in patients with cirrhosis from chronic viral hepatitis maybe determined by a number of factors including viral and disease activities, the degree of fibrosis/cirrhosis and host factors including concomitant diseases. The recent AASLD guideline advocates describing stages of cirrhosis based on varices and ascites. Stages one and to represent compensated cirrhosis, whereas the latter two stages indicate hepatic decompensation. Prognosis in patients with hepatic decompensation maybe assessed by systems such as Child Pugh classification or MELD score.

Accumulating data indicate that antiviral treatment can modify the prognosis of patients with cirrhosis. This includes prevention of progression, regression of fibrosis and reduction of HCC risk.
standardized cirrhosis mortality rate decreased by 22%. Variations in cirrhosis mortality at the country level reflect differences in prevalence of risk factors such as alcohol use and hepatitis B and C infection. Treatment of this disease is expensive and largely inaccessible in most parts of the world. Fortunately, preventive measures (screening transfused blood, introducing hepatitis B vaccination programs, reducing alcohol consumption) are relatively inexpensive. Therefore, cost-effective National health policies are urgently required to control and reduce risk factors.

Although LC is the end-stage disease leading to death, it is not a terminal disease but a dynamic process. Therefore, diagnosis before decompensation and specific treatments when applicable, are important steps towards reducing the mortality of end-stage liver disease. Patients with cirrhosis should be treated when possible for the underlying liver disease to stop disease progression.

The increasing burden of liver disease and the problem of late presentation with decompensation emphasize the need for population screening to identify patients with chronic liver disease. Adequate treatment with antiviral drugs changes the natural history of liver disease even after the onset of major decompensation in patients with chronic HBV or HCV infection. As noninvasive tool such as transient elastography has shown high accuracy in diagnosing liver cirrhosis at early compensated status, it is very important to diagnose cirrhosis at reversible status and manage to not to progress by reducing or eliminating risk factors.
Canada lacks a national HCV strategy. Recent proposals by the Public Health Agency recommends, contrary to most other countries/regions such as the USA and Europe, that universal screening for HCV not take place.
Indeed, not even ‘baby boomers’ are recommended for screening, only those with an admitted risk factor such as previous history of injection drug use, incarceration, immigration from a high-endemic region, receipt of blood products, etc. Many Canadian treating physicians and others have argued against such an apparently misguided and inappropriate decision.

The exact prevalence of HCV in Canada remains unclear. Estimates suggest that somewhere around 0.7-0.9% of the population of 35 million is infected (260,000 – 320,000). The genotypes found are 1a (40%), 1b (18%), 3 (25%), 2 (12%), 4 (4%), 6 (2%). The variability of genotypes is predominantly due to immigration: 3 is predominant in West Asians, some aboriginal and IVDU populations; 4 is found in immigrants/migrants from the Middle East and Africa, and 6 is from SE Asia. Estimates suggest that anywhere from about half to 2/3 of HCV-infected persons are aware of their positive status. However, these are only speculations based on incomplete and potentially unreliable data.

Canada is one of the few countries where those infected through the blood supply before 1990 have been awarded financial compensation by the government, in amounts up to $300,000 USD if they have advanced disease or died of liver-related complications such as HCC or endstage liver failure.

A national database registry has been organized, to track some of the HCV therapy outcomes including longterm outcomes such morbidity, mortality, return to work. This registry is called CANUHC (Canadian Network Undertaking against Hepatitis C).

Currently approved regimens include almost all the DAAs including: sofosbuvir-based regimens such as ledipasvir+SOF, velpatasvir+SOF; daclatasvir+asunaprevir; grazoprevir+elbasvir; and the 3-D regimen with paritaprevir, ombitasvir, dasabuvir. Approval for glecaprevir+pibrentasvir is expected in the summer of 2017. Although the ‘list price’ of these regimens is expensive, in the range of about $45,000 USD for a 12-week course, the health regions (provinces) have recently negotiated a secret discounted price, details of which are known only to the pharma companies and the ministries of health, for a much lower price, based on some type of progressive and incremental discount strategy, thought to be “the more you use, the less you pay” per patient treated. According to estimates, less than 50,000 HCVinfected individuals have been cured by antiviral therapy to date.
Hepatic Encephalopathy (HE) is a complex and potentially reversible neuropsychiatric syndrome characterized by a wide spectrum of neuropsychiatric abnormalities that range from mild disturbances in cognitive function and consciousness to coma and death. The occurrence of the first episode of HE in a cirrhotic patient is a pejorative prognostic factor, and constitutes a turning point in the evolution of liver disease. Estimated survival rates are 42% at 1 year, and 23% at 3 years. Although a clear pathogenesis is yet to be determined, elevated ammonia in serum and the central nervous system is the mainstay for pathogenesis and treatment of HE. Enteric flora generates the production of additional neurotoxic molecules, such as phenols, mercaptans, and short-chain fatty acids, which potentialize the toxic effects of ammonia. Additional mechanisms involved in HE include modifications of the blood–brain barrier, disruptions in neurotransmission and abnormalities in GABAergic and benzodiazepine pathways.

Clinical guidelines for HE were published years ago, and many physicians have developed comfort with older therapies. As new therapies are discovered, practice patterns should change. The first step in treatment is identifying and treating precipitating causes, including but not limited to hypovolemia, gastrointestinal (GI) bleeding, infection, dehydration secondary to diuretic use, diarrhea, vomiting, hyponatremia, hypokalemia or hyperkalemia, alkalosis, surgery, renal failure, TIPS, constipation, benzodiazepine use, narcotic use, hypoxemia, hepatoma, and noncompliance with lactulose therapy. Non-absorbable disaccharides, such as lactulose, have traditionally been regarded as first-line pharmacotherapy for patients with HE. However, multiple adverse events have been associated with their use. In addition, recent literature has questioned the true efficacy of the disaccharides for this indication. Neomycin, metronidazole and vancomycin may be used as alternative treatments for patients intolerant or unresponsive to nonabsorbable disaccharides. Antimicrobials reduce bacterial production of ammonia and other bacteria-derived toxins through suppression of intestinal flora. Neomycin has been reported to be as effective as lactulose, and similar efficacy has been reported with vancomycin and metronidazole for the management of HE. However, the adverse effects frequently associated with these antimicrobials limit their use as first-line pharmacological agents.

Rifaximin is a novel antimicrobial agent with a wide spectrum of activity that has shown promise as an alternative antimicrobial treatment option for HE. Rifaximin showed superior efficacy compared with lactulose for the treatment of HE, similar efficacy to paromomycin, and similar or greater efficacy than neomycin. Rifaximin was found to be associated with fewer hospitalizations, fewer days of hospitalization, and lower hospitalization charges than were seen with lactulose. Rifaximin also had a better tolerance profile than the comparative agents. Newer ammonia scavengers and orally ingested activated charcoal are being studied. Glycerol phenylbutyrate is a new compound that is a prodrug of sodium phenylbutyrate with much lower therapeutic doses needed. It is being evaluated for type C HE and has done well in trials for urea cycle disorders. Orally ingested activated charcoal (AST-120) is also being explored for the treatment of HE. Probiotics are not as useful in OHE but have been used with some success in minimal HE. The species that are most efficacious are Lactobacilli and Bifidobacteria. Other less frequently utilized...
alternative treatment options include administration of benzodiazepine receptor antagonists, branched-chain amino acids, ornithine aspartate, zinc supplementation, sodium benzoate, dopamine receptor agonists, acarbose and extracorporeal devices for liver dialysis. Presently, there is relatively limited clinical data supporting their routine use in HE. Some patients with persistent HE despite removal of precipitating factors and treatment with currently available medical therapies may have extensive portosystemic shunting. These shunts may be embolized via percutaneous catheterization.
The aim of this study is to clarify the efficacy of oral direct-acting antiviral agents (DAAs) for chronic hepatitis C (HCV) genotype 1 as well as the risk factors for developing hepatocellular carcinoma (HCC) after achieving sustained virological response (SVR) in chronic hepatitis C patients.

Overall, 641 patients enrolled in Japan with HCV-1 received Daclatasvir (DCV)/Asunaprevir (ASV) for 24 weeks, and 530 patients received sofosbuvir (SOF)/ledipasvir (LDV) therapy for 12 weeks. Resistance-associated variants (RAVs) in the HCV NSSA and NS5B regions were assessed at baseline and virological relapse by direct sequencing. Serum M2BPGi, α-fetoprotein (AFP), Fib4 index were measured at pre-treatment (pre-Tx) and post-treatment (post-Tx; SVR24) in patients with and without prior HCC.

Overall, 86.9% (543/625) of patients had SVR12 by DCV/ASV therapy, which was significantly higher in NSSA 93Y (wild) (88.3%) compared with NSSA 93H at baseline (48.0%). SVR rates by SOF/LDV did not significantly differ between patients with and without NSSA Y93H/N [94.2% (113/120) vs. 97.7% (347/353)], but the SVR rate was significantly lower in patients with prior DCV/ASV therapy than those without it [69.2% (18/26) vs. 98.4% (496/504), \( P < 0.001 \)]. In the SVR patients without the history of HCC, older age, male gender, advanced fibrosis, high AFP or M2BPGi were associated with HCC development (21/496, 4.2%), while those with prior HCC had no significant difference of baseline characteristics, but higher tendency of AFP and M2BPGi was found in the recurrence group (53/152, 34.9%). Cumulative carcinogenesis rates in history of HCC group were 30% and 37% after 1 and 2 year, while 4% and 5% in no history of HCC group. The cumulative carcinogenesis rate significantly differed between these groups (\( p < 0.001 \)).

SVR rates by DAAs therapy are high except for re-treatment of IFN-free DAAs therapy. However, past history of HCC, male gender and high AFP and M2BPGi levels at the time of SVR24 were the risk factors for HCC development in patients after HCV eradication by IFN-free regimen.
KEYNOTE LECTURE IV

Chairs

Professor Barjesh Chander Sharma
Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Professor Sheikh Mohammad Fazle Akbar
Toshiba General Hospital, Tokyo, Japan

Professor Gamal Shiha
Egyptian Liver Research Institute and Hospital (ELRIAH)
Although various drugs and management strategies have been developed and recommended for treatment of chronic liver diseases of different etiologies, the clinical efficacies of these approaches and real life implications are far from being satisfactory.

On the basis of retrieved evidences, we developed an immune therapeutic strategy for chronic hepatitis B (CHB) that used both HBsAg and HbcAg (NASVAC) in higher doses (200-400 micrograms) for 15 times via nasal and injection routes in CHB patients. The safety and efficacy of NASVAC were ascertained in HBV transgenic mice and normal control subjects. These were followed by comparison of safety and efficacy of NASVAC with those of pegylated interferon (Peg-IFN) in a phase I/II/III clinical trial in 160 patients with CHB (Intention to Treat). At end of treatment (EOT) and during follow up, it appears that NASVAC is either better or comparable to Peg-IFN regarding antiviral, liver protection, and arrest of fibrosis in CHB patients. NASVAC induced both HBsAg and HbcAg-specific immunities in CHB patients and HbcAg-specific immunity played a cardinal role for therapeutic effect of NASVAC.

Based on our studies for treatment of CHB patients, an inference was developed that antigen-specific immunity may be safe and effective for broad range of patients and this exposed an area of tackling liver diseases due to HCV, liver cirrhosis, autoimmunity, and HCC by using antigen-specific immune therapy.

Preclinical trials have been initiated or on designing for almost all forms of chronic liver diseases so that more insights develop for tackling future agendas of immune therapy for chronic liver diseases and its complications including HCC.
Novel therapy of HCC

Chair:
Professor Chinburen Jigjidsuren
Director of National Cancer Center, President of MHPB Society

Chair:
Professor Jinsil Seong
Department of Radiation Oncology, Yonsei University College of Medicine, Seoul, South Korea

Professor Shagdarsuren Manaljav
Mongolian Academy of Sciences, Shagdarsuren Hospital
Image-guided percutaneous ablation has been widely performed on patients with HCC, generally for those with Child-Pugh A or B who have three or fewer tumors each 3 cm or less in diameter. Randomized controlled trials have demonstrated that radiofrequency ablation (RFA) is superior to ethanol injection (Shiina S, et al. Gastroenterology 2005). In our 10-year experience of RFA, 5- and 10-year survival rates were 60.2% and 27.3%, respectively. Multivariate analysis demonstrated that age, anti-HCV, Child–Pugh class, tumor size, tumor number, serum DCP level, and serum AFP-L3 were significantly related to survival. Five- and 10-year local tumor progression rates were both 3.2%. Five- and 10-year distant recurrence rates were 74.8% and 80.8%, respectively. (Shiina S, et al. Am J Gastroenterol 2012). It is obvious that sophisticated RFA is a curative treatment and enables long-term survival in HCC.

RFA is, however, highly operator-dependent. Its skills and outcomes are different from operator to operator. Juntendo, the highest volume center of RFA in Japan, have held RFA training programs to disseminate skills and knowhows for RFA. In eight domestic programs, 130 Japanese doctors participated while in three international ones, 31 foreign doctors attended. The programs were composed of lectures, live demonstrations and case studies. Lecture contents were current status of RFA, RFA devices, ultrasonography, and others. In live demonstrations, RFA was performed on cases of a tumor below the diaphragm requiring artificial ascites, a tumor in the caudate lobe, a tumor adjacent to the heart, a portal vein or hepatic vein, a tumor over 5 centimeters, more than five tumors, hepatic metastasis, etc. We demonstrated importance to have appropriate patient posture, usefulness of our original dedicated probe for interventional procedures and our dedicated operation table, and ways to perform ablation under Sonazoid guidance, and with multimodality fusion imaging. In case studies, difficult to ablate cases from participants’ hospitals were presented and discussed. Questionnaire surveys revealed overwhelmingly positive feedback. Our programs may be useful to provide opportunities to understand basic concepts and learn essential technical tips in RFA.

Various innovations, such as dedicated US transducers for interventional procedures, dedicated procedure bed, contrast-enhanced ultrasound, multimodality fusion imaging, and new ablation systems like new-generation microwave ablation systems would further improve outcomes in ablation. Sophisticated ablation would be superior to conventional surgery.
vessel invasion, mostly portal vein tumor thrombosis (PVTT) are classified as
Barcelona Clinic Liver Cancer (BCLC) stage C, where sorafenib is recommended as a standard of care according to the BCLC guidelines but with unsatisfactory survival outcome.

Radiotherapy (RT) hasn’t been recognized as the standard of care due to lack of controlled phase III trials. However, numerous studies have demonstrated that RT not only causes tumor responses but also provides prolonged survival in this group. Significant responses after RT in patients with HCC and PVTT have been reported, and the objective response rate of PVTT was 39-62%. In several reports, the RT responder group showed significantly longer survival than the non-responders and the response to RT was an independent prognostic factor associated with better survival in multivariate analysis. These results suggest that RT can be an effective treatment that brings significantly improved local control and survival. Although previous studies demonstrated that RT is a promising approach, the median survival in these studies did not reach 1 year. The small number of patients in these studies was not sufficient to define the factors contributing to treatment response. Furthermore, the radiotherapeutic schemes were heterogeneous depending on the institutions, which make the optimal treatment strategy uncertain. These issues need further investigation to improve the therapeutic outcome of patients with HCC and PVTT.

Recently, we performed a nationwide, multicenter study for a total of 985 patients investigating treatment outcomes as well as the optimal radiotherapeutic strategy in patients with hepatocellular carcinoma (HCC) and portal vein tumor thrombosis (PVTT). Through the study we found that the equivalent RT dose 45 Gy, given in combination with other treatments, provided better PVTT control and OS. The optimal RT volume is suggested for either PVTT + primary or PVTT only.

Taken together, RT can provide a significant therapeutic benefit for HCC patients with PVTT. The efficacy can further be improved by multimodal treatment with higher RT dose.

**OS 7-2: Multimodality Treatment of Hepatocellular Cancer**

Patients with hepatocellular carcinoma (HCC) complicated by major
tumor and patient factors in terms of tumor number, size and liver function
resulting in various outcomes given by transarterial chemoembolization (TACE). Transarterial radioembolization (TARE) using radioactive isotope, β-ray emitting Yttrium-90 with a short half-life and penetration depth, is an emerging intra-arterial brachytherapy characterized by potent anti-cancer effect given by radiation but minimal embolic effect. Although there is lack of study directly comparing the efficacy and safety between TACE and TARE in patients with unresectable HCC, several retrospective or small-scaled studies suggest that overall efficacy indicated by overall survival and time to progression is similar between two modalities and TARE has a superiority in the safety including postembolization syndrome, hospitalization days and outpatient-based therapy. In advanced HCC with portal vein (PV) invasion, TACE is not consistently recommended due to risk of hepatic decompensation or failure after procedure. On the contrary, available data suggest that TARE might be a promising treatment option in HCC with PV thrombosis if patient’s liver function is preserved and the level of PV invasion is less than main trunk. Ongoing trials comparing TARE and sorafenib in advanced HCC would elucidate the role of this locoregional therapy. The need of a multidisciplinary team, complex steps of procedure and high cost of TARE are the hurdles to widespread recommendation of this therapy in intermediate or advanced HCC. The optimization of selection between TACE and TARE might be dependent on availability, experience, tumor factors and patient factors.

There is a similarity between TARE and external beam radiation therapy (EBRT) because radiation effect is the key in killing tumor cells in both modalities. However, there are also several differences in terms of delivery of radiation, dose, treatment duration and adverse events.

Another emerging transarterial therapy for HCC is drug-eluting beads (DEB) TACE, and there have been many reports to compare the efficacy and safety between conventional and DEB-TACE.

In this presentation, the clinical outcomes of emerging transarterial therapies focused on TARE and DEB-TACE will be discussed.

Hepatocellular carcinoma (HCC) of intermediate stage consists of diverse
Sunday, June 18, 2017

Professor Mamun Al Mahtab
Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Professor Yasuhito Tanaka
Department of Virology & Liver Unit, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan
Liver failure can present as acute liver failure (ALF; in the absence of chronic liver disease or cirrhosis, and is associated with a high 28-day mortality. The APASL definition is a simple bedside tool, which enables a clinician to stratify a patient presenting with liver failure for early intervention to slow the progress or reverse the failure and improve survival. The APASL ACLF Research Consortium (AARC) established in 2012, has more than 56 collaborative centers and have collected nearly 3,250 patients in a short span. On the other hand the Western (CLIF SOFA) definition involves an acute deterioration of pre-existing chronic liver disease, usually related to a precipitating event and is associated with increased mortality at 3 months due to multiorgan failure. Spesis and organ failure are integral part of the Western definition of ACLF accordingly.

Acute insults include alcohol, hepatotropic viruses and drugs whereas the underlying chronic liver disease is generally cirrhosis due to alcohol, hepatitis B or C, or NASH. Chronic liver disease/ cirrhosis could be diagnosed by presence of signs or imaging features of PHT, transjugular liver biopsy or HVPG. The pathophysiology of ACLF relates to persistent inflammation, immune dysregulation with initial wide-spread
immune activation, a state of systematic inflammatory response syndrome and subsequent sepsis due to immune paralysis. The disease severity and outcome can be predicted by both hepatic and extrahepatic organ failure(s). A short ‘golden window’ of 7 days precedes sepsis development and organ(s) failure, and provides opportunity for immunomodulation with GCSF and other interventions; extrahepatic organ failure indicates severity of illness, prognosis and helps guide management. In fact, if patients have a bilirubin of above 15, INR >2.5 and hepatic encephalopathy, the patients have high mortality and risk of development of sepsis increases upto 10% every day.

Clinical recovery is expected with the use of nucleoside analogues for hepatitis B, and steroids for severe alcoholic hepatitis and severe autoimmune hepatitis. Artificial liver support systems (Liver dialysis using MARS or Prometheus and Plasma exchange) help remove toxins and metabolites and serve as a bridge to liver transplantation. Hepatic regeneration during ongoing liver failure, although challenging, is possible through the use of growth factors such as GCSF and EPO. Liver transplantation is the definitive treatment and a good outcome is achieved with early transplantation in carefully selected patients. Patients with a MELD of ≥25 and a delta MELD of >4 points in 7 days should be considered for early liver transplantation. The results of liver transplant are good with nearly 85% one year survival.

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PGC 1-2: HCV Therapy with Peg-Interferon and Ribavirin in Myanmar: A Resource Constrained Country

To investigate peg-interferon (peg-IFN) and ribavirin (RBV) therapy in Myanmar and to predict sustained virologic response (SVR).

**Professor**

**Gfy 1**

Honorary Professor,

Yangon, Myanmar

This single-center, open-label, study was conducted in Myanmar between 2009 and 2014. A total of 288 patients infected with HCV genotypes 1, 2, 3, and 6 were treated with peg-IFN alpha-2a (180 μg/week) or alpha-2b (50 to 100 micrograms as a weight-based dose) and RBV as a weight-based dose (15 mg/kg/day). Treatment duration was 48 weeks in genotypes 1 and 6, 24 weeks in genotype 2, and 24 or 48 weeks in genotype 3 based on rapid virologic response. Those co-infected with hepatitis B received 48 weeks of therapy.

**Results:**

Overall, SVR was achieved for 82% of patients and was well tolerated. All patients achieved SVR at equivalent rates regardless of HCV genotype (p = 0.314). Low fibrosis scores (p < 0.001), high baseline albumin levels (p = 0.012), and low baseline viral loads (p = 0.065) all independently predicted SVR. On the other hand, IL-28B TT and CC genotypes were not found to significantly predict SVR (p = 0.634; p = 0.618). The occurrence of RVR showed a >96% positive predictive value (PPV) for achieving SVR. Treatment duration did not significantly impact the likelihood of achieving SVR for patients infected with genotype 3 HCV (p = 0.371). The most common adverse events were fatigue 71% and poor appetite 60%. Among
SVR rates were high with peg-IFN and RBV therapy in Myanmar. Fibrosis scores, baseline albumin, HCV RNA levels, and RVR independently predicted SVR.

Patients with genotype 3 HCV, more patients in the 48-week treatment group required erythropoietin compared to the 24-week treatment group (61.1% vs. 49.2%).

Conclusion:
SVR rates were high with peg-IFN and RBV therapy in Myanmar. Fibrosis scores, baseline albumin, HCV RNA levels, and RVR independently predicted SVR.

Professor Shiv Kumar Sarin
Hepatology and Director, Institute of Liver and Biliary Sciences, New Delhi, India

Sunday, June 18, 2017
09:40-10:00

PGC1-3: Management of Refractory Variceal Bleeding

Acute variceal bleeding (AVB) is a medical emergency and associated with a mortality of 20 to 40% at 6 weeks and is defined as presence of hematemeses within last 24hr of presentation, and / or ongoing melena, with last melenic stool within last 24hr. According to the APASL consensus published in 2011, the AVB is further classified as active or inactive at the time of endoscopy. Combination therapy with vasoactive therapy- Terlipressin, somatostatin or octreotide, should be given immediately (<30min of hospitalization, ‘Door to Needle Time’) combined with endoscopic variceal ligation (‘Door to Scope Time ‘ <6 hrs) and is effective in about 80-85% patients. Failure to control bleeding is defined as fresh hematemesis with in 2 hr of combination of vasoactive drugs + EVL, >2 g drop in Hb (6% drop in Hct) without transfusion and hemodynamic instability. This failure, is considered as refractory variceal bleeding and requires immediate change in therapy. Predictors of failure to control bleeding include high hepatic venous pressure gradient (HVPG) >20 mmHg, active spurter, infection, high MELD and portal vein thrombosis. Patients not responding to the combination therapy should undergo early emergency TIPS, specially if the HVPG is >20 mmHg, even in patients with advanced liver disease. In patients with MELD >15 however, TIPS may not improve survival despite control of bleed. Now a good alternative is the use of Ella Danis stent, a self expanding metal stent. These stents are quite effective in controlling post-EVL ulcer bleed and can be removed easily after a week or two. In 7 of our last 8 patients, the bleed could be controlled. In our experience of more than 70 cases, the success in control of refractory variceal bleed is 95%, with survival of 63%.

Antibiotic prophylaxis is recommended and search for acute ischemic hepatic injury should be done. Ischemic hepatitis (IH) develops in about 10% of cirrhotics following AVB; more so in Child’s C patients and is associated with higher mortality. N acetyl cysteine (NAC) therapy in a recent study at ILBS has shown to significantly ameliorates the development of severe IH and decreases the incidence of AKI, though was not found to reduce mortality.

Gastric varices are present in about 20% of patients with portal hypertension with a reported incidence of bleeding of about 25% in 2 years, with a higher bleeding incidence for IGV1 and GOV2. High risk varices are >10mm, Child class (C>B>A), and endoscopic presence of variceal red spots. Use of N-butylycnoaocrylate glue or TIPS is recommended for control of acute
GV bleed and for secondary prophylaxis. Balloon retrograde obliteration of varices (BRTO) and TIPS can be used in patients with failure to control GV bleed.

Sunday, June 18, 2017 10:00-10:20

PGC 1-4: Innovative therapies in Hepatology

In the era of DAAs when hepatitis C is likely to be conquered, hepatitis B still remains a concern, as we are yet to have in our armory any antiviral against hepatitis B, which is not too inferior compared to the DAAs. With this background we have conducted phase I/II and phase clinical trials of a new generic, “NASVAC”, which has been registered in Cuba recently.

 Decompensated cirrhosis the sequel of chronic hepatitis B, as well as any other chronic hepatitis. It is characterized by significantly high mortality, but available therapeutic options are limited. Liver transplantation remains the only definitive therapy. Limited availability of donor organs and prohibitive cost is however concern. Liver support device (MARS) only serves as a ‘bridge’ to transplant, not reducing mortality significantly compared to standard medical treatment. We are testing the possibility of mobilization of bone marrow derived stem cells, i.e. CD34 cells, with repeated G-CSF injections, harvesting these cells using plasmapheresis machine and then re-transfusing large number of these CD34 cells through trans-hepatic arterial or trans-femoral venous or trans-cubital venous routes. So far 23 patients with decompensated cirrhosis, irrespective of aetiology, have been treated, which establishes the safety of this evolving therapy to counter liver cirrhosis.
6th HCV conference
APASL Single Topic Conference 2017
16 - 18 June • Ulaanbaatar • Mongolia

POSTGRADUATE COURSE II
FOR MONGOLIA DOCTORS

Chairs
Professor Jazag Amarsanaa
Scientific Committee Chairman

Professor D. Badamsuren
Department of Gastroenterology, 3rd Central Hospital
“Элэг бүтэн Монгол” хөтөлбөрийн зорилго нь Монгол улсын хүн амын евчлэл, нас баралтын тэргүүлэх шалтгааны нэг болж буй элэгний хатуураал, элэгний хавдрын евчлэл нас баралтыг буруулах у нийн Dr. тулээ элэгний евчний шалтгаан болсон элэгний вирусин халдварт нь тархалтыг хяналтад авах явдал юм.

“ЭЛЭГ БҮТЭН МОНГОЛ” хөтөлбөрийн хүрээнд үе шаттайгаар дараах ажлыг хийнэ. Үүнд:


2. Өрх, сумын эрүүл мэндийн төвд хийсэн шинжилгээгээр элэгний В, С вирусийн халдвартай илэрсэн бол эрүүл мэндийн даатгалын ёренхий газраас итжээлэгдсэн лабораторуудад вирус тээвэр шинжилгээнд хамруулна.

3. Элэгний В, С вирус тээвч болон элэгний архаг евчтай, хатуураалтай иргэд байвал элэгний хорт хавдрыг эрт илрүүлэх үзлэгт хамруулна. Эрт илрүүлэг үзлэг өрх буй зорилтот булгийн хүнд элэгний ЭХО, хавдрын маркер AFP тодорхойлох шинжилгээ, биохимийн болон цусны хэлбэрэн шинжилгээнд хамруулна. Уг элэгний хорт хавдрын өнгүүлэх багц шинжилгээг аймаг, дуурийн тувшинд хийж эхэлд төлөөлөөнд байгаа.

4. Ус тээвэр шинжилгээгээр вирусийн архаг тээвч өмчилгөөгий хийх архаг шаардлагатай иргэдийг хүндрүүлэхээр вирусийн эсрэг шинжилгээнд хамруулах. Элэгний архаг шаардлагатай болон элэгний вирус тээвч хүндрүүлэх өмчийн хяналтанд бүрэн хамруулагч шаардлагатай онцлохой, өмчилгөөгээ зааврын дагуу хийх юм.

5. Элэгний хорт хавдрын илсэн хүндрүүлэг Хавдар Судлалын Төв хорт хавдрны өмчилгөөг удирдамжийн дагуу хийх зорилготой хөтөлбөр юм.

6. Элэгний хавдрын эхний шат, элэгний хатуураалтай, зайлгүй элэг шилжүүлэн суулгах шаардлагатай иргэдийн элэг шилжүүлэн суулгахаа санхүүжилтийг тер харицуулаа.

Sunday, June 18, 2017 10:45-11:05
HBV infection is a serious global public health problem with 250-350 million people chronically infected. It accounts for 500,000-1.2 million deaths per year and is the 10th leading cause of death worldwide. The prevalence of HBV infection varies markedly in different geographic and in different population subgroups. Highly endemic areas are sub-Saharan Africa and Asia. Mongolia is endemic area for HBV infection and estimated around 200,000 people chronically infected. Universal vaccination was shown to be cost-saving in countries with high and intermediate endemicity.

Diagnosis of HBV infection and of HBV-related liver diseases is traditionally based upon the assessment of virological, serological markers as well as liver function tests, imaging techniques, non-invasive tests for fibrosis and liver biopsy.

Antiviral therapy of chronic HBV infection is aimed to stop viral replication in order to improve patient survival by preventing progression cirrhosis, endstage liver disease or hepatocellular carcinoma. Current therapies of chronic hepatitis B remains limited to either pegylated-interferon-alpha, or one of the five approved nucleoside analogues (NAs) treatment.

While viral suppression can be achieved in the majority of patients with high-barrier-to-resistance new-generation NAs, HBsAg loss is achieved in only 10% of patients with both classes of drugs after a follow-up 5 years. Therefore, there is a renewed interest to investigate a number of steps in the HBV replication cycle and specific virus-host cell interactions as potential targets for new antivirals. There will brief introduce about it.
Professor

Head of the Outpatient Department,
National Center for Communicable Disease
Sunday, June 18, 2017
11:05-11:25

PGC 2-3: Монгол улс дах харьцангуй эрүүл хүн амын дундах вирүст хепатитын тархалтын судалгааар 11-16% хепатитын С вируусийн эсрэг бие илэрч байгаа нь хепатитийн С вируусийн тархалт өндөр хувьтай байгааг харуулж байна.

ХСВ-ийн халдвартай яав, тавилан нь вируусийн генотипыг хамаардаг болохыг дэлхийд олон эрдэмтэд тогтоосон бөгөөд ХСВ-ийн генотип нь улс ундэтээн бүрт үдээр ам ирээтэй хэв хэвэн ирлээ. Монгол улсын дундах вирүст хепатитын түрүүдийн 95-98% бөгөөд вирүст хепатитын эмчилгээнд ийлж болсон нь мөн дэлхийд байна. 2015-2016 оноос ЭМСЯ-аас Хепатитийн С вируусийн илрүүлэг, оношлогоо, эмчилгээний зааврыг боловсруулж 2016 нд А/249 тоот тушаалаар шинэчлэл баталсан. Монгол улсад 2015 оноос асс нь 12 сар овогдоо эмчилгээнд хэрэглэж өндөр талаар архаг зөвлөлдөө монгол түрүүдийн 95-98% бөгөөд вирүст хепатитын эмчилгээнд ийлж болсон нь мөн дэлхийд байна.
элэгний хатууралгүй өвчтөнд 3 сар, элэгний хатууралтай өвчтөнд 6 сар үргэлжилцүүлэн.

2015 он 12 сарын 1-ны өдөр ХӨСҮТ халдварт эмч нарын хяналт нь хепатитийн C вирусийн эсрэг софосбувир/ледифасвир эмчилгээг ЭМЯ-аас батлан гаргасан илрүүлэн, оношлогооны зааврын дагуу хийж эмчилүүлэхдийн хяналтын картанд дүгнэлт хийж 647 өвчтөнд хийсэн судалгаагар эмчилгээний үр дүнг (SVR) тооцож эмчилгээ дууссаны дараа 12 дахь долоо хоногт вирусийн ачааллыг тодорхойлоход элэгний архаг үрэвсэлтэй хүмүүст 98%, элэгний хатууралтай хүмүүст 95% байсан.

Уг судалгаагар эмчилгээнд хамрагдсны 56,2%-д гаж нөлөө илрээгүй, илэрсэн гаж нөлөөөндөөс толгой ордох 21,6%, ядрах 19,18%, нойронд муу болох 1,8%, ус унах, дотор муухайрах, суулгах илэрэх зэрэг шинжүүд 0,22%-д илэрсэн.
The hepatitis delta virus (HDV) is a defective RNA virus requiring the presence of the HBV for the completion of its life cycle. The origins of this virus remain unknown, although some recent studies have suggested an ancient African radiation. The age of the association between HDV and HBV is also unknown.

With very few countries in the world suffer from co- and super-infections of HBV and HDV, this infection is still considered one of neglected diseases in the world. And Mongolia is one of endemic countries with still high prevalence of HDV, which draws attention of virologists and hepatologists.

This lecture reviews specific aspects of hepatitis delta virus (HDV) reproduction, including virion structure, the RNA genome, the mode of genome replication, the delta antigens, and the assembly of HDV using the envelope proteins of HBV. HDV evolution, prevention, virus entry, HDV diagnostic approaches, current and future treatment options will be covered. The only established management of CDH consists of conventional or pegylated interferon therapy, which has to be administered at doses used for hepatitis B for a duration of at least 1 year. Posttreatment week-24 virologic response is the most widely used surrogate marker of treatment efficacy, but it does not represent a sustained virologic response, and late relapse can occur. Alternative treatment options are an urgent need in CDH.

Clinical characteristics of chronic HDV infection and possible complications will be discussed as well.
Professor

Department of Gastroenterology, 3rd Central Hospital

төө эрс цөөрч, элэгний хэвийн бутэц байгуулагч гэмтэн, холбооч эдийн хатуураа, захилгаат бүрдэл үүсч, элэгний дутмагшлаг, үүдэн хураагуурын даралтын ихэлэлээд хүрээд гарах, даахдад үйцэн эмгээгийг элэгний цирроос гэнэ.

Эсийн үржил нэмэгдэхээ, эсийн бичил бутэц томрох, эсийн гаднах зай нэмэгдэдээ, хэсэг газрын өөрчлөллүүдээс элэг томорно.

Дэлдээ тоомрсноор зэрэглэлээг эрэхийг дарах шахахын зэрэгээд үүдэн болон цусны бага зэрэглэлэн түүний үйл ажиллагаагаанд өөрчлөл түүний үйл ажиллагаагааны үзэлтэд үүсч. Захын үйл ажиллагааны үзэлтэд үүсч, үүдэн хүрээд гарах шахахын зэрэгээд үүдэн болон цусны бага ажиллагаагаанд өөрчлөл түүний үйл ажиллагаагааны үзэлтэд үүсч. Захын үйл ажиллагааны үзэлтэд үүсч, үүдэн хүрээд гарах шахахын зэрэгээд үүдэн болон цусны бага ажиллагаагаанд өөрчлөл түүний үйл ажиллагаагааны үзэлтэд үүсч.
It’s reported that stage of liver cirrhosis, macro and micro vascular
invasion, portal vein tumor thrombus and cancer stage are associated with the postoperative recurrence of hepatocellular carcinoma (HCC). In this study, we aimed to investigate the anti hepatitis C virus (HCV) treatment impact on the recurrence of HCC (hepatocellular carcinoma) after curative resection or RFA (radiofrequency ablation) treatment.

Methods:
Patients with active HCV related HCC who had undergone curative hepatectomy or RFA were enrolled and analyzed to clarify the significance of anti HCV treatment at National Cancer Center of Mongolia. All patients were preoperative and postoperative HCV-RNA level of higher than 1000 IU/mL.

Results:
The recurrence rate in patients who had received anti HCV treatment was significantly lower than in those without anti HCV treatment (P = 0.02).

Conclusion:
The patients with HCV treatment after curative liver resection or RFA showed lower recurrence rate than without HCV treatment patients. Antiviral therapy is recommended, especially for patients who underwent curative hepatectomy for HCV-related HCC to decrease the recurrence of HCC.
POSTER EXHIBITION
Acute Hepatitis A, B and C but not D is Still Prevalent in Mongolia: A Time Trend Analysis

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Background: Mongolia has one of the highest viral hepatitis A, B, C and D infection incidences worldwide.

Objective: We sought to investigate changes in the proportion of acute viral hepatitis types in Mongolia over the last decade.

Methods: The cohort comprised 546 consecutive patients clinically diagnosed with acute viral hepatitis from January 2012 to December 2014 in National Center for Communicable Diseases, Ulaanbaatar, Mongolia. A time trend analysis investigating the change in proportion of acute hepatitis A virus (HAV), hepatitis C virus (HCV), hepatitis B virus (HBV), and hepatitis D virus (HDV) infection among the cohort with respect to a previous published study was undertaken.

Results: Acute hepatitis A, B and C was diagnosed 50.9%, 26.2%, and 6.0% of the cohort. Notably, 16.8% of the cohort had a dual infection. The etiologies of acute viral hepatitis were varied by age groups. The most common cause of acute viral hepatitis among 2-19 year olds was hepatitis A, HBV and superinfection with HDV among 20-40 year olds, and HCV among 40-49 year olds. Patients with more than one hepatitis virus infection, were significantly older, more likely to be male and had a higher prevalence of all risk factors for disease acquisition. These patients also had more severe liver disease at presentation compared to those with mono-infection.

Conclusions: Acute viral hepatitis is still prevalent in Mongolia. Thus, the need for proper infection control is increasing in Mongolia.

HCV/HBV co-infection: epidemiology, clinical characteristics, viral interactions and mortality
Background: Because of the shared modes of transmission, HCV/HBV co-infection is not uncommon, especially in endemic areas and among subjects with a high risk of parenteral transmission. Patients with dual HCV/HBV have a higher risk of progression to cirrhosis and decompensated liver disease with an increased risk of hepatocellular cancer (HCC). HCV/HBV co-infected patients represent a diverse group with various patterns of viral replication.

Objective: The aim is to summarize the risk factors and epidemiology of HCV/HBV co-infection and to describe its clinical characteristics in two medical centers for period of 2012-2016.

Methods: In total 408 patients with chronic viral hepatitis C (HCV) with mean age of 52 (range 27-77) years were examined. HCV/HBV was diagnosed in 25 (6%) of them, 19 (80%) were men. In this study we prospectively assessed serological, virological, biochemical parameters and instrumental investigations. The mean MELD score was 22.6±3.2 (13-47).

Results: The prevalence of hepatitis B (HBV) co-infection in a total of 408 patients with chronic HCV was 6%. Injection drug use was the predominant risk factor for dual HCV/HBV (85%). Higher rate of liver cirrhosis (LC) 20 (80%) and decompensated liver disease (Child-Pugh class C 40%) were reported in co-infected patients. Two of them were diagnosed with chronic hepatitis, three with HCC. Male sex, previous alcohol abuse and older age (>60) were predictors for developing of HCC in co-infected cirrhotic patients. The following complications were revealed in patients with liver disease decompensation: ascites in - 10 (40%), Hepatic encephalopathy in 5(20%), variceal bleeding-in 4 (16%), Hepatorenal syndrome (HRS) – in 4(16%). The patients with combined HBV/ HCV showed the following spectrum of virological profiles: 18 (72%) of HBV/HCV co-infected patients appeared to have high replication of HCV and inactive HBV replication, 4 (16%) - high HBV DNA levels and undetectable HCV RNA, three others presented active replication of both HCV/ HBV. The overall mortality was 20%, the main causes of mortality were HE (30%) and HRS (25%).

Conclusions: HCV /HBV dual infection is a complex clinical/virological entity. Decompensated liver disease were reported in (40%) of coinfected patients

The HCV replication was higher in most of coinfected patients (72%)
The mortality was associated with complications of HE and HRS
The correct assessment of HBV and HCV replication is mandatory for proper therapeutic approach.

Gender differences in liver disease progression by ethnicity in patients with...
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Studies of gender differences in HCV infection are limited. Our aim is to characterize gender differences in HCV infection in an ethnically diverse United States patient cohort.

Consecutive HCV patients were identified via ICD 9 query with data obtained by individual chart review. The study included 9,142 patients 3551 female (387 Asian, 3164 Non-Asian) and 5591 male (487 Asian, 5104 Non-Asian).

Males and females had similar in age (54±11 vs 54±12, p = 0.23) but males were more likely to have a history of tobacco (65% vs 51%) and alcohol (34% vs 27%) use (p<0.0001), as well as cirrhosis (44% vs 35%), decompensation (31% vs 24%) and HCC (11% vs 5%) at presentation than females (p=0.001); however antiviral treatment rates (33% vs 33%) (p=0.89) and SVR (37% vs 38%) were similar to (p=0.01). Within Asians, males were more likely to be younger (59±13 vs 61±15) (p=0.04) have a history of tobacco (48% vs 13%) and alcohol (24% vs 8%) use (p<0.0001), have cirrhosis (47%vs 41%) (p=0.09), decompensation (36% vs 30%) (p=0.06), and HCC (26% vs 15%) at presentation (p<0.0001); however antiviral treatment (52% vs 51%) rates and SVR (46% vs 48%) remained similar (p=0.82). Among NonAsians, males were more likely to be older (58±10 vs 53±12, p=0.004), have a history tobacco use (67% vs 56%, p < 0.0001), less likely to have a history of alcohol use (30%vs35%, p =0.01), and more likely to have cirrhosis (44% vs 35%), decompensation (31%vs 24%), and HCC (9% vs 4%) than females at presentation (p< 0.0001 for all). In contrast, antiviral treatment (32% vs 33%) rates and SVR (36% vs 37%) were similar (p=0.51). Within Asians, males had a lower 5 (32% vs 34%) and 10 (46% vs 48%) year incidence of HCC, and 5(28% vs 24%) and 10( 39% vs 38%) year incidence of HCC, and 5(28% vs 24%) and 10(39% vs 38%) year incidence of HCC, and 5(28% vs 24%) and 10(39% vs 38%) year incidence of decompensation although the results were not statistically significant. Males overall had higher 5(19% vs 15%, p=0.01) and 10(44% vs 40%, p = 0.004) year incidence of hepatic decompensation than females. Males overall also had statistically significantly higher rates of progression to cirrhosis and HCC with similar trend seen between Non-Asian males and females.

Males were more likely than females to develop liver complications related to HCV infection on both Asian and Non-Asian patients. Patients of both ethnic groups should be especially monitored and treated prevent long-term complications.

Polymorphism of genes involved in the reactions of congenital immunity, while viral hepatitis C in ethnic groups of Buryats and Mongolians

Background and objective: In Mongolia, there is a phenomenon of absolute dominance of 1b virus genotype of - 98.8% (Baatarkhuu O. et al., 2008). In ethnically close Buryatia, its concentration does not exceed 54.8% (Malov S.I. et al., 2012), and in neighboring China - 56.8% (Gower E. et al., 2014). A possible explanation for the existing phenomenon may be the presence of a genetic predisposition of the population to the 1b genotype, in which this clone of the virus receives a selective advantage when distributed in Mongolia. The aim of this study was to test the proposed hypothesis by the study of the SNP genes IFNL4 (rs368234815), IFNL3 (rs12979860 and rs8099917), CD209 (rs4804803), TLR3 rs3775291 and rs13126816 in cohorts of Mongolian patients with hepatitis C virus and in the ethnically similar Buryat group, and also in patients with Hepatitis C caused by different virus genotypes.

Methods and Result: A total of 400 patients with chronic HCV were examined, including 200 from the Republic of Buryatia and 200 from Mongolia. The compared groups of patients completely matched in clinical-laboratory and sexage indices. There were no associations of polymorphic variants of the genes CD209, IFNL3, and ethnicity of patients, as well as genotypes of the virus in the Buryat population. Obviously, the internalization of different genotypes of the virus into the cell is universal, and, at least, does not depend on the polymorphism of the CD209 gene. In contrast, as a result of the work performed, two SNPs in the candidate genes TLR3 (rs3775291) and IFNL4 (rs368234815) were detected, polymorphic variants of which occur with different frequency in patients with 1 and not 1 (2/3) genotypes of the virus. Carriers of G-allele rs3775291 TLR3 are 3.1 times more resistant to infection with 2/3 virus genotypes (p <0.0001), and carriers of ΔG-allele rs368234815 IFNL4 - 2.0 times (p <0.02). Consequently, the higher the proportion of human carriers of these alleles and their haplotypes in a population, the higher the tolerance for the spread of 2/3 genotypes of the virus in it. Under these conditions, the first genotype of the virus will receive genetically determined selective advantages, displacing the 2nd and the 3rd from circulation.

Conclusion: Further studies at the level of practically healthy people in Mongolia and Buryatia, as well as the inclusion of other polymorphisms in the analysis will help establish the role of congenital immunity genes in the selective selection of individual genotypes of the virus. The study was carried out with the financial support of the RFBR grant No. 16-54-44047.

Diversity of the association of serum levels and genetic variants of MHC class I polypeptide-related chain A with liver fibrosis on chronic hepatitis C

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Background and objective: Genetic variants of rs2596542 of MHC class I polypeptide-related chain A (MICA) have been associated with hepatocellular carcinoma (HCC). The linkage between serum MICA (sMICA) and liver fibrosis in chronic hepatitis C (CHC) is elusive.

Methods: SNP rs2596542 of MICA and sMICA was tested for the association with liver fibrosis in 319 biopsy proven CHC patients.

Results: Linear regression analysis revealed that factors independently correlated to sMICA were α-fetoprotein (β: 0.149; 95% confidence interval [CI]: 0.001, 0.003; P = 0.007) and MICA rs2596542 GG genotype (β: 0.209; 95% CI 0.153, 0.483; P < 0.001). While patients were stratified according to their MICA genetic variants, advanced fibrosis was the only factor independently correlated to sMICA (OR/CI: 2.996/1.428-6.287, P = 0.004) and platelet counts (OR/CI: 0.988/0.982-0.994, P < 0.001) on MICA rs2596542 A allele carriers.

sMICA > 50 pg/mL provided a positive predictive value of 72% in predicting advanced liver fibrosis (F34) and of 90% in significant fibrosis (≥F2).

Conclusions: Levels of sMICA were highly correlated to liver disease severity in CHC patients who carried the MICA rs738409 A allele. Patients possessing the genetic predisposition had a higher likelihood of significant liver fibrosis if they expressed higher sMICA levels and may be considered as a high priority of antiviral treatment.

**Hui-Ying Rao**, **Hong Li**, **Feng Chang**, **Hong Chen**, **Jia Shang**, **Qing Xie**, **Zhi-Liang Gao**, **Jun Li**, **Lai Wei**

Objective: Hepatitis C viral (HCV) infection is a threat to public health and curing the disease is an efficient way to manage the infection source. With the availability of direct acting anti-viral (DAA), the question becomes at what price we are willing to eliminate the disease. This research aims to make a comparison of cost per sustained viral response (SVR) in treating HCV between interferon based therapy and DAA in Mainland China.

Methods: SVR data of IFN based therapy come from a 5-year prospective follow up cohort of 512 Han ethnic patients (i.e., the CCgenos Study); SVR data of DAA (daclatasvir plus asunaprevir, or Dual DAA) come from a phase III randomized but open labeled trial among HCV genotype 1b patients either intolerance or ineligible to IFN therapy in Mainland China, South Korea, and Taiwan China. Price of IFN is taken from Mainland China (a 52-week treatment to non-cirrhosis is 54,860 RMB or 9,143 USD) while price of DAA (Dual DAA) for a
24-week treatment is taken from Taiwan China (249,984 NTD or 8,248 USD) since Dual DAA has been just approved in Mainland China without a price; Dual DAA is already marketed in Taiwan China.

Among 1b patients, the PegIFN treatment SVR24 was 62.4% while SVR24 for the DAA treatment was 91.2%. Applying the pricing information, this research finds that for IFN based treatment, cost per SVR24 is 23,482 USD and for DAA (Dual DAA) treatment, cost per SVR24 is 10,014 USD.

For every successful SVR24 achieved, DAA (Dual DAA) treatment not only takes 50% less in time, in comparison to IFN based therapy, but DAA (Dual DAA) is almost 60% less expensive: for every successful SVR24, DAA (Dual DAA) has 13,468 USD in saving. As Dual DAA is the first DAA approved in Mainland China and more DAAs are expected to be approved soon into the country, this difference, both in clinical outcomes and finance, can be very meaningful at a country level helping to make health policy regarding HCV. In conclusion, to Mainland China healthcare system, using DAA to replace IFN based therapy is an economically attractive approach to eliminate HCV as a public health threat.

There is no sponsorship to this research from any pharma company
There were totally 647 patients received Harvoni for HCV infection by September 2016. People who received treatment for less than 3 months there 31% and for longer than 3 months were 8%. Among them 91.9% have chronic hepatitis and first stage of liver cirrhosis and 8% have liver cirrhosis and carcinoma. After 1 month of treatment, HCV RNA tests result was negative for 98.8% of all Harvoni patients and for the rest 1.1% resulted in decrease of HCV RNA. After 3 month of trerapy, blood test result showed 100% recovery on transaminase level. 453/465, 10/465 and 2/465 of them were respectively genotype 1b, 2 and 1a. APRI score were pre-treatment 1.3±0.58 and post treatment 0.443±0.148. FIB4 score were pre-treatment 3.8±1.2 and post treatment 1.65±0.59. Occurrences of side effects were mild. 1.2%, 5.8% and 4.6% of them were respectively with CTP C, CTP B and CTP A scores.

88.2% of the participants were chronic hepatitis C and 1.7% of them were pre-treated by interferon. After treatment by Harvoni tablets, excellent SVR12 results were shown among the study participants’ and the favorable side-effect profile were observed for the Mongolian context.

The prevalence of cryoglobulinemia in patients with chronic hepatitis C infection

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Hepatitis C virus (HCV) infection has been reported 10-70% prevalence of cryoglobulinemia in different countries. We have studied the prevalence of cryoglobulinemia and factors associated with cryoglobulinemia in chronic hepatitis C (CHC) patients.

This report included 2577 treatment naïve patients from a University Hospital and designed to assess the related factors for cryoglobulinemia in CHC. Demographic features, biochemical analyses, and serum cryoglobulinemia precipitation were collected in baseline. Estimated glomerular filtration rate (eGFR), AST to platelet ratio index (APRI) and fibrosis index based on four factors (FIB4) calculated for the study.

857 (32.5%) of the 2577 patients were positive for in cryoglobulin. By univariate analyses, cryoglobulinemia positive patients are older (55.0±11.2 vs. 51.7±11.4 years; p <0.0001), lower HCV-RNA load (5.3±2.1 vs. 5.8±2.2 log IU/ml; p<0.0001), lower triglycerides (88.0±38.0 vs. 108.7±66.2 mg/dL; p<0.0001), lower cholesterol (165.6±33.8 vs. 169.8±33.1 mg/dL; p=0.014), lower platelet (161.3±67.7 vs. 172.4±59.3 10⁹/L; p<0.0001), higher GOT level (97.4±57.9 vs. 91.6±62.8 U/L; p=0.025), higher eGFR (96.8±27.2 vs. 88.0±25.4 mL/min; p<0.0001), higher APRI (1.63±1.34 vs. 1.42±1.34; p <0.0001) and higher FIB4 (3.62±2.7 vs. 2.97±2.58; p<0.0001) compared to cryoglobulinemia negative patients. The proportion of female patients in cryoglobulinemia positive group was higher (54.8% vs. 41.3%; p<0.0001). By multivariate logistic regression model age (Odds Ratio [OR] = 1.03; 95% Confidence Interval [CI]: 1.01-1.04; p<0.0001), female gender (OR = 1.37; CI: 1.08-1.72; p=0.008), HCV-RNA load (OR = 0.93; CI: 0.89-0.98; p=0.008), triglycerides...
(OR = 0.992; CI: 0.990-0.995; p<0.0001) and eGFR (OR = 1.02; CI: 1.01-1.02; p<0.0001) was associated with cryoglobulinemia.

Our findings suggest the prevalence of cryoglobulinemia is 32.5% CHC patients and associated with older age, female gender, low HCV-RNA load, lower triglycerides and renal function.

998

Screening program for early stage of liver cancer

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Incidence of liver cancer is 4th rate of common cancers and 3rd rate of deaths due to cancer incidence in the world. In the Mongolia, cases of liver cancer are 37.7% of all cancer cases and mortalities are 43.3%, which is the first leading cause of mortality among cancer. In our country, 81.2% of the liver cancer is diagnosed at its late stages (stage 3 or 4) and the 5-year survival rate (after diagnosed) of 19.5%, are associated with lack of high-risk population screening. The most common causes of liver cancer are hepatitis B and C virus, liver fibrosis and cirrhosis.

Screening and diagnosis in early stage of liver cancer in high-risk population group

In our study we used single center patient data. These patients are controlled in screening in early stage of liver cancer in Happy Veritas Clinic and Diagnostic Center. In this center, patients are included for HCC screening, when they have liver fibrosis stage higher than F2 (over 7.2 kPa) that indicates higher likelihood of developing HCC. Fibrosis stage was measured using a FibroScan (Fibroscan 502 Touch, Echosens, Paris, France). The total number of patients included for screening was 10682 patients such as abdominal ultrasound and to identify serum alfa fetoprotein (AFP) every 3 months. 181 patients were included in the study, who had complete set of data, and are regularly controlled for screening in early stage of liver cancer. Medical history, results of blood test, liver function tests, AFP, liver fibrosis stage (TE) and abdominal ultrasound examination results were collected for each patient.

181 patients with an average age of 54 ± 11 (range: 23 - 89 years old) were included in the study. In the result, causes of liver fibrosis were HCV 59.1% (107), HBV 24.9% (45), HBV/HDV 13.3% (24), HCV/HBV 2% (3), HCV/HBV/HDV 0.6% (1) and without hepatitis viruses 0.6% (1). According to the study, F2 stage was 64.6% (117), F3 stage 27.1% (49) and F4 stage 8.3% (15). We studied the changes in laboratory tests and depending on the patient’s fibrosis stage. Increasing fibrosis stage or liver cirrhosis has decreased platelets, albumin and total protein level (p<0.001). However, we observed alanine aminotransferase level, which increased in F3 stage and decreased fibrosis stage F4. Liver cancer nodule is detected in 4 patients from 181 participants during the follow-up. Those 4 patients had fibrosis stage F4 in Fibroscan analysis and average level of AFP was 86.
We conclude that patients in F4 stage in Fibroscan analysis have higher risk of developing liver cancer. Therefore, health care providers need regularly screening and testing in early stage of liver cancer in high risk population.

This study will be a valuable part of National strategy of early detection of liver cancer developed by Ministry of Health and WHO.

**Title:** WFA⁺-M2BP in CHC patients

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**Objective:** We assessed its efficacy in evaluating liver fibrosis stage and disease progression in CHC in Taiwan.

**Methods:** A total of 229 patients with CHC who underwent liver biopsy and serological tests for WFA⁺-M2BP were enrolled. The association between WFA⁺-M2BP and clinical outcome was evaluated according to the liver fibrosis stage. We also aimed to find the factors that affected the WFA⁺-M2BP level in CHC.

**Results:** According to the metavir scoring system, there were 23 patients (10.0%) of f0, 62 (27.1%) of f1, 56 (24.5%) of f2, 38 (16.6%) of f3, and 50 patients (21.8%) of f4, respectively. The mean levels of wfa⁺-m2bp was 3.02 ± 3.08 (range= 0.26 -5.53) in f0, 2.23 ± 1.76 (0.11-8.06) in f1, 3.45 ± 3.37 (0.16-14.30) in f2, 3.48 ± 3.73 (0.35-14.3) in f3, and 3.77 ± 3.70 in f4 (0.46- >19.78), respectively. The optimal cutoff values of wfa⁺-m2bp for fibrosis stages ≥f1, ≥f2, ≥f3, and f4 were 1.42, 1.61, 1.42, and 2.67, respectively. The accuracy for significant fibrosis (≥f2), advanced fibrosis (≥f3), and cirrhosis were 62.1%, 53.3%, and 65.0%, respectively. The linear regression analysis between significant liver fibrosis stage (≥f2) and wfa⁺-m2bp revealed significant trend (b = 0.19; 95% confidence interval [ci]: 1.057-1.374; p=0.005).

**Conclusion:** Wfa⁺-m2BP is a simple and reliable noninvasive marker for liver fibrosis assessment in CHC patients.
Pegylated IFN-α 2a plus ribavirin combination therapy results in Mongolian patients with hepatitis C virus genotype 1b

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Background: Mongolia is one of the highest prevalent of hepatitis C virus infection of the world. The standard therapy for patients with genotype 1 chronic hepatitis C (CHC) is a combination of peg-interferon alfa-2a and ribavirin for 48 weeks. However the most appropriate duration of treatment remains to be established because of treatment–related side effects and cost.

Objective: To compare the efficacies of 24-week and 48-week treatments of peg-interferon alfa-2a plus ribavirin in Mongolian patients

Methods: A total of 47 patients with genotype 1 CHC was treated between August 2008 and were randomly assigned to treatment and December 2013 and at least one dose of study medication, consisting of 180 mg of peginterferonalpha 2-a once weekly plus daily ribavirin (1000 or 1200mg, depending on body weight). Patients with undetectable HCV RNA at 24 weeks of treatment were allowed to choose either 24 or 48 weeks as the duration of their treatment; 4 patients chose the 24 week treatment regimen and the 43 patients chose the 48-week regimen.

Results: The SVR rate was higher in patients treated for 48 weeks than in those treated for 24 weeks (74% vs 48.8%, p=0.0013). In the multivariate analysis, age <52 years, platelets >148000mm3, and treatment duration for 48 weeks remained significant independent predictors of SVR. For the 47 patients who relapsed in the 24-week treatment group received split 24-week therapy, and 3 patients was achieved SVR. The overall SVR rate did not differ significantly between the 24-week treatment group, including those who underwent 24-week split therapy 48.8%, and the 48-week treatment group (48.8% vs 74%).

Conclusion: SVR rate was 74% of the patients in Mongolia. The 24-week therapy following failure is a useful treatment strategy for patients with genotype 1b chronic hepatitis C.

Multicenter study on outcome of HCV treatment using Ledipasvir/Sofosbuvir

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Background: The incident of liver cancer in Mongolia generally caused by HBV and HCV, and it is 7 times higher than that of world average. HCV, the most prevalent cause of HCC in Mongolia, is number one public health issue. Mongolia is one of the first countries that registered Ledipasvir/Sofosbuvir (LDV/SOF) regimen from developing countries. By the support of Access program run by Gilead Sciences, USA, we started HCV treatment program from January 2016.

Method: We followed and evaluated treatment outcome of patients with HCV infection using combination of 90mg ledispavir/400mg sofosbuvir (manufactured by Gilead Science) in 937 treatment naïve and 83 treatment experienced patients. All patients were treated with LDV/SOF for 12 weeks and, their treatment was evaluated by quantitative HCV-RNA assays prior and W (week) 4 and W12 of treatment. Sustained virological response (SVR) after 12 weeks treatment was assessed. Virus genotype analysis using cDNA microarray, liver enzymes, CBC and drug related adverse events were assessed in every patient. The laboratory tests were conducted at National Center of Communicable Diseases, Happy Veritas Laboratories and other provinces’ health care center.

Results: We conducted largest ever (415/1020) HCV genotype (GT) distribution study in Mongolian chronic HCV patients. 96,6% (n=401) of assessed patients were GT1b; 0,7% (n=3) were GT2; 0,2% (n=1) were GT1a and b; 0,9% (n=4) were GT1b and 2; 0,5% (n=2) were GT1b and 6;0,2% (n=1) were GT5 and 0,2% (n=1) were GT1b and 80k mutants respectively.992/1020 (97,3%) patients achieved SVR12W, 28 (2,7%) patients who did not achieve SVR12W were all genotype 1b. Median ALT level significantly dropped during treatment from 95,5±84,1 IU/Lto 27,2±18.6 IU/L and slightly increased by the end of treatment 42,9±17,4IU/L. Total of 39 adverse events were observed in 595/1020 patients (58,3%). Single adverse events were observed in 401/1020 (39,3%) whereas 2 and more events were observed in 194 (19%) patients respectively.Unreported adverse events such as partial facial palsy, AFP (alpha-fetoprotein) increase, melasma were observed.

Conclusion: Treatment of HCV in Mongolia using all-oral dual DAA was divided in 3 phases due to shortness of drugs and logistics arrangements. We were able to include only stage-one patients in this study. We achieved 97,3% SVR12W for 3 months treatment with LDV/SOF this time. But viral relapse has to be determined.
repeatedly at weeks 24 and 48 post treatment. All viral relapses (n=14) and non-responders (n=14) were GT1 in our study. According to HCV genotype assessment, there was no difference in treatment outcomes between patients who had different genotypes. Genotype distribution of Mongolian patients confirmed the results of other smaller studies. HCV RNA clearance during treatment was no different than clinical trials, but the slight increase of ALT by the end of treatment was commonly observed. It might have happened due to rebound of immune reaction after clearance of HCV or a drug induced effect.

The efficacy of combined Sofosbuvir and Daclatasvir in treating hepatitis C patients – a preliminary report

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The combination of sofosbuvir and daclatasvir can be used for treating all genotypes of hepatitis C. As such, genotype testing can be skipped making this combination more attractive for hepatitis C elimination protocols. The combination of both drugs in a single tablet (Sovodak) has been first available in Iran and is being tested in this study.

The aim of the study is to include 1000 subjects with hepatitis C including subjects with cirrhosis, co-infection with HIV or HBV, renal failures, and post-transplant subjects. Patients are treated with a single fixed dose combination pill containing 60 mg daclatasvir and 400 mg sofosbuvir (Sovodak 60/400, RojanPharma, Tehran, Iran) taken once daily for 12 weeks. For subjects with cirrhosis, weight-based ribavirin (1000 mg daily if less than 75 kg or 1200 mg if 75 kg or over) is also added. If ribavirin is contraindicated or not tolerated, the treatment will be extended to 24 weeks with Sovodak alone. The dose of daclatasvir is modified to 30 or 90 mg (Sovodak 30/400 or Sovodak 90/400) in subjects on anti-retroviral treatment (HIV) if required due of drug interaction. Subjects with renal failure receive the same treatment (without ribavirin) but are followed weekly. Response to treatment was assessed 12 weeks after the end of treatment with a sensitive assay (SVR12).

Until now over 680 subjects have been enrolled, 440 have finished the treatment and 267 have been followed for 12 weeks after end of treatment (time frame for SVR12). So far 79% of our patients are male and 52% have cirrhosis. The mean age is 50 years and the mean pre-treatment viral load is 4,287,000 IU/mL. The most common genotype is genotype 1 (56%) followed by genotype 3 (41%). Four cases had multiple genotype infection (1 and 3 or 3 and 4) and 3 were untypable. Of the 267 patients who have finished the follow-up period 259 have responded to treatment (97.0%, SVR12). The SVR rate for cirrhotic and non-cirrhotic patients was similar at 97%. Side effects included headache, fatigue, and diarrhea and pruritic rash. None of these side
effects was severe enough to require dose modification or discontinuation of treatment. Of particular interest is lack of side effects in renal failure patients, even those under hemodialysis.

According to guidelines, the combination of sofosbuvir and daclatasvir can be used to treat all genotypes of hepatitis C. The literature indicates an SVR rate of above 95% for non-cirrhotics which is comparable to our results. But the rate of SVR in cirrhotic patients is around 80-85% in the literature whereas the SVR observed in our subjects has been much better at 97%. Currently the most difficult to treat population is genotype 3 cirrhotic patients. The SVR for this group has been 96.3% in our study which is a very good number. The better response of Iranian patients has also been observed in older studies evaluating the efficacy of pegylated interferon and ribavirin. It appears that Iranian patients are somewhat easier to treat. The same might be true in other Asian countries as reported by some researchers.

Considering the results of this study and the ease of use (one pill a day) we believe Sovodak can be the best choice for treating all cases of hepatitis C in Iran. Due to the uniformity of treatment regimens across genotypes it might not even be necessary to check the genotype in the future. This is especially useful in nation-wide elimination programs where the elimination of any single test would have an enormous effect on the budget. This fact, combined with the low price of Sovodak, makes this treatment very attractive for HCV elimination programs. Pilot studies for HCV elimination are already underway in Iran using this combination.

**902**

A novel single daily fixed dose combination of sofosbuvir 400 mg + ribavirin 1000 mg + EGCG 400 mg is superior to the standard of care as an anti-viral and safer causing less hemolysis in patients with chronic hepatitis C

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Chronic Hepatitis, the leading cause of liver disease, infects more than 185 million people worldwide, ideally, inhibitors should target different steps of the HCV infectious cycle, entry, replication, and assembly/secretion and be efficient against all HCV genotypes. Therefore, the development of novel, netter-rolerated, and more-effective anti-HCV agents is utgently needed. The novel patented EHCV (Catvira) formulation composed of Sofosbuvir 400mg/Ribavirin 1000mg/Epigallocatechin Gallate 400mg (EGCG) was developed. Catvira formulation incorporated EGCG for its anti-hemolytic and effective inhibitory activity against viral entry into human host cells. We evaluated the efficacy and safety of a single daily fixed dose EHCV (Catvira) in comparison to the standard of care (Sofosbuvir 400mg + Ribavirin 1000mg) multiple tablets per day in CHC genotype 4 patients.

Randomized open-label study was carried out on treatment-naïve and treatment-experienced patients with genotype 4 HCV infection (No.=80) were randomly assigned to receive a single daily fixed dose EHCV (40 patients) or the standard of care Sofosbuvir + Ribavirin (40 patients) daily for 12 or 24 weeks.
SVR 12 and SVR 24 for EHCV (Catvira) showed no statistical significant difference when compared to the standard of care (P<0.1 & P<0.2 respectively). Also EHCV (catvira) demonstrated a much faster rate of viral load decline (P<0.01) which could be due to effective viral entry inhibition into human host cells by EGCG. Moreover EHCV (Catvira) did not affect RBCs count or Hemoglobin levels as compared to the standard of care that resulted in a significant decline (P<0.05) in both parameters after 24 weeks of treatment. This could be attributed to the anti-hemolytic effect of EGCG.

Catvira, administered daily for 12 or 24 weeks, is safe and effective in both naïve and treatment experienced patients with genotype 4HCV. Catvira’s anti-viral-entry mechanism may also play a role in enhancing efficacy over the standard of care. In addition to potentially enhanced efficacy, Catvira’s anti-hemolytic activity may improve the safety and tolerability of the therapy. Being a single daily dose of Catvira is another advantage leading to better compliance.

A real world cost effectiveness analysis of interferon-based therapy for HCV naïve

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Objectives:
Direct-acting antiviral (DAA) era in hepatitis C virus (HCV) treatment is coming. Unfortunately, the availability and affordability of DAAs in Asia-Pacific areas vary, making it difficult to develop a universal HCV practice guideline appropriate for the whole Asian population. This study aimed to evaluate the realworld cost-effectiveness of IFN-based therapy according to the current strategies with PegIFN/RBV for “easy-to-treat” to provide a reference for application of future DAA develop for IFN-eligible, treatment naïve HCV patients.

Methods:
A total of 1,032 chronic hepatitis C treatment-naïve patients who corresponded to response-guided therapy (RGT) guideline of PegIFN/RBV regimens were linked to the entire population of expenditures and order in the National Health Insurance Research Database of Taiwan. The average total cost per SVR achieved was calculated as the summation of the total cost for all treated patients /number of SVR cases.

Current RGT suggested 24 weeks of PegIFN/RBV for G1 naïve patients with baseline LVL and RVR at treatment week 4 achieved1, the average treatment cost per SVR was $5,090±2,400. It was of superior cost-effectiveness compared with those other subgroups of G1 patients. In terms of G2 patients, according to current RGT of 16 weeks of treatment duration, PegIFN/RBV treatment with RVR achieved was of a very competitive cost per SVR ($3,237±488).
For a naïve patient in the new DAA era, the PegIFN/RBV will might be conserved for those with all favorable risk parameter, considering the treatment duration and cost per SVR, in the resource-constrained countries.

The comparative study of cirrhosis stage in patients with HBV infection and HBV/HDV co-infection

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There are about 350 million people with HBV infection in the world. 5% or about 15-20 million people of them are co-infected HDV. Every year an average of 7500 people are detected HDV new infection and 1,000 people die due to HDV infection in the United States. The Middle East, Pakistan, Central and Northern Asia, Japan, Taiwan, some areas of Africa, Greenland Amazon Basin and Pacific region have high prevalence of HDV infection. North America, Northern Europe, Southern Africa and East Asia have low prevalence of HDV infection. There is 70-90% higher risk of liver cirrhosis in patients with HBV/HDV co-infection than patients with HBV infection.

Comparative study of cirrhosis stage in patients with HBV infection and HBV/HDV co-infection

Our study continued from January 2015 to March 2017 and we measured liver fibrosis stage in patients with HBV infection and HBV/HDV co-infection using a FibroScan (kPa) (Fibroscan 502 Touch, Echosens, Paris, France), who are controlled in Happy Veritas Clinic and Diagnostic Center. When we measured liver fibrosis stage in 5504 patients with HBV infection, 20% or 1115 of the patients is determined HDV co-infection. In our study, in random sampling cases are selected 354 patients with HBV single infection and HBV/HDV co-infection. 177 of all patients have HBV/HDV co-infection. We selected parameters from patient medical histories in our study, such as serologic markers of HBV, quantification of HBV and HDV in serum samples, blood test, liver function test and liver fibrosis stage. Summary statistics were performed using SPSS 22.0 software.

354 patients (169 men (47.7%) and 185 females (52.3%); range (18-75)) are participated in our study. According to the comparative study in laboratory tests, ALT level was HBV - 44 (36; 51.5) and HBV/HDV - 61 (39.8; 97.55). AST level was HBV - 39.1 (30; 83) and HBV/HDV - 50 (33.1; 77.8). The Platelet count was HBV - 193±66 and HBV/HDV 181±62.8.

When we compared, liver fibrosis stages were HBV - F0 67 (37.9%), HBV/HDV - F0 57 (32.2%), HBV - F1 22 (12.4%), HBV/HDV - F1 17 (9.6%), HBV - F2 39 (22%), HBV/HDV F2 39 (22%), HBV - F3 29 (16.4%), HBV/ HDV - F3 41 (23.2%), HBV - F4 20 (11.3%) and HBV/HDV - F4 23 (13%). In table 1 shows the difference of liver fibrosis by age group.

Table 1. Liver fibrosis result of Fibroscan by age group
**HCV therapy with peg-interferon and ribavirin in Myanmar: a resource constrained country**

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To investigate peg-interferon (peg-IFN) and ribavirin (RBV) therapy in Myanmar and to predict sustained virologic response (SVR).

This single-center, open-label, study was conducted in Myanmar between 2009 and 2014. A total of 288 patients infected with HCV genotypes 1, 2, 3, and 6 were treated with peg-IFN alpha-2a (180 μg/week) or alpha-2b (50 to 100 micrograms as a weight-based dose) and RBV as a weight-based dose (15 mg/kg/day). Treatment duration was 48 weeks in genotypes 1 and 6, 24 weeks in genotype 2, and 24 or 48 weeks in genotype 3 based on rapid virologic response. Those co-infected with hepatitis B received 48 weeks of therapy.

Overall, SVR was achieved for 82% of patients and was well tolerated. All patients achieved SVR at equivalent rates regardless of HCV genotype (p = 0.314). Low fibrosis scores (p < 0.001), high baseline albumin levels (p = 0.012), and low baseline viral loads (p = 0.065) all independently predicted SVR. On the other hand, IL-28B TT and CC genotypes were not found to significantly predict SVR (p = 0.634; p = 0.618). The occurrence of RVR showed a >96% positive predictive value (PPV) for achieving SVR. Treatment duration did not significantly impact the likelihood of achieving SVR for patients infected with genotype 3 HCV (p = 0.371). The most common adverse events were fatigue 71% and poor appetite 60%. Among patients with genotype 3 HCV, more patients in the 48-week treatment group required erythropoietin compared to the 24-week treatment group (61.1% vs. 49.2%).

SVR rates were high with peg-IFN and RBV therapy in Myanmar. Fibrosis scores, baseline albumin, HCV RNA levels, and RVR independently predicted SVR.
Prevalence of hepatitis B and C Virus in particularly healthy population of Ulaanbaatar city

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Hepatitis B (HBV) and C virus (HCV) are one of the major causes of liver cirrhosis and hepatocellular carcinoma (HCC) in Mongolia. More than 77% of the Mongolian population is estimated to have been infected with hepatitis B virus (HBV) at some time during their life, and between 10% and 22% of the general population is chronically infected with either hepatitis B or C. In 2015, liver cancer accounted 39.1% of the all newly registered cancer and comparing to last year it is increased by 4 percent and taking highest rank.

Objective:
This study was designed to determine the prevalence of anti-HCV antibody and HBsAg in apparently healthy population of Ulaanbaatar city, Mongolia

Methods:
Four thousand people who lives’ in Ulaanbaatar city were included in this study. The rapid immunochromatographic test was applied for detection of HCV antibodies and HBV combo rapid test. Data were reported as frequency and percentage and analyzed using SPSS software version 17.0 for Windows.

Results:
A total of 4000 participants with age range of 11-86 years and mean ± standard deviation of 38 ± 13 years, including 2077 males (52%) and 1923 females (48%) were enrolled in this study. In Table 1 shows study participant’s general information, including age group. The anti-HCV prevalence was 10% (n=392), HBsAg positive was 8% (n=343) and HBsAb positive was 32% (n=1280). And 0.5% of participants had a coinfection of hepatitis C virus and hepatitis B virus. The median age for positive anti-HCV test was 46 ± 14. When the anti-HCV positive subjects were categorized by decade of age, the prevalence in each age group was as follows: 4% in teens, 4% in 20’s, 7% in 30’s, 12% in 40’s, 19% in 50’s and 32% in subjects >/=61 years of age. The prevalence of anti-HCV had a tendency to increase with age. For HBV, the median age for positive HBsAg test were same 38 ± 12. The prevalence in each age group was: 3% in teens, 9% in 20’s, 9% in 30’s, 10% in 40’s, 9% in 50’s and 8% in subjects >/=61 years of age. The peak prevalence of HBsAg (10%) was observed among persons 41 to 50 years of age.

Discussion:
In 2008, the prevalence of chronic HCV infection in Mongolia was strikingly high considering that the 15.6% in the apparently healthy population (O.Baatarkhuu et al., 2008). In our findings, the prevalence of chronic HCV infection decreased to 10%. Approximately 8% of apparently healthy population had a HBsAg positive and 32% had a HBsAb positive. Although high prevalence of HBV and HCV in Ulaanbaatar, Mongolia. This high prevalence of hepatitis virus in Mongolia in older people is attributed to the reuse of phlebotomy needles and needles for injection before 1990’s (Ebright et al., 2003). These day contaminated equipments used in health-related procedures, particularly in dental and surgical manipulations, probably play predominant roles in transmission of virus hepatitis (D.Davaalkham et al., 2012).
Elbasvir, Grazoprevir; with or without Ribavirin and its effectiveness with Sofosbuvir resulting SVR in chronic hepatitis C genotype 1 prior experienced co-infected individuals. A randomized open label clinical prospective trial:

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Background: Oral directly acting anti-viral therapy has virtually cured Chronic Hepatitis C. However, for a few subgroups (genotype 1,3 and 4 with co-infection with HIV) in HCV remain challenging. Also baseline resistance associated variance in genotype 1a and 3 need longer duration of therapy.

Objective: Study evaluates the safety and SVR of Elbasvir, Grazoprevir; with or without Ribavirin and its effectiveness with Sofosbuvir

Methods: Twenty-two patients recruited from 2014-2016 from community with prior experience to HCV therapy. Exclusion: Liver transplant, HCC, HBV, Hemoglobinopathies (Sickle cell), HIV RNA undetectable, CHF, Renal insufficiency, prior allergy to DAA’s, cirrhosis of liver with MELD > 12, sepsis, cardiomyopathy, active IVDU, active cocaine, no family support, non-compliant to drug rehab program, Major depression, decompensated affective disease, treatment failure prior because non-compliance, high dose PPI

Prior DAA failure: n=7 were on Harvoni, n=8 were on Olysio, n= 5 Viekera Pak, n=2: Sofosbuvir plus Ribavirin. All HIV co-infected individuals were on Atripla; while few were also on Raltegravir. Further subdivided into two groups:

Group A (n= 10): Elbasvir 100 mg + Grazoprevir 50 mg + Sofosbuvir 400 mg for 12 weeks

Group B (n= 12): Elbasvir 100 mg + Grazoprevir 50 mg + Sofosbuvir 400 mg for 12 weeks with RBV 600 mg a day

Patient Characteristics:

Group A (n = 10) Mean age 59, Genotype 1a(n = 5),1b (n = 5),Mean HCV viral load 4.7 million, Mean CD4 count 560,Mean HIV viral load 3699. Out of the total 10, past response rate was unknown in 4/10, 3/10 were partial responders and 3/10 were relapers.

Group B ( n = 12 ) Mean age 58, Genotype 1a (n =6), 1b (n = 6),Mean HCV viral load 3 million, Mean CD4 count 436,Mean HIV viral load 387. Out of the total 12 , past response rate was unknown in 4/12, 4/12 were relapers,3/12 were partial responders and 1/12 was non responder.

Results:

In group A HCV RNA load became undetectable in 8/10 by week 4 and 10/10 by week 8,Retention was 100% and ITT was 100%.Mean hemoglobin and ALT remained stable through out 24 weeks. In group B HCV RNA load became undetectable in 10/12 by week 4 and 11/12 (91.67%) by week 8. One patient withdrew due to shortness of breath and chest pain. Retention was 91.67% and ITT was 100%.Mean hemoglobin and ALT remained stable remained stable throughout 24 weeks.

Side Events: Fatigue, Nausea, Vomiting, Headache, Anemia (group B 9/29), Insomnia, Diarrhea, Constipation, UTI Abdominal pain, Hematuria, Renal Stone, Gouty attack, Hypoglycemia, Hyperglycemia, URI, Dysgeusia, Pruritus, Pneumonia (Group B, stopped meds and got hospitalised)

This clinical trial reveals promising SVR in a very selective Cohort of Chronic Hepatitis C Co-Infection in Prior experienced population with severe fibrosis and significant morbidities. A larger trial needs to validate.

Integrated analysis of controlled clinical trials evaluating efficacy and safety of sofosbuvir-based regimens in chronic hepatitis C genotype 6 (HCV GT 6)


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HCV GT 6, the most diverse genotype with 28 subtypes to date, affects approximately one-third of patients with HCV infection in Southeast Asia and immigrants in Europe and North America coming from that region. Few studies have examined the efficacy and safety of direct-acting antiviral (DAA) regimens in these patients, and most are limited by small sample sizes. The aim of this study is to provide an integrated analysis of safety and efficacy from clinical trials of SOF-based regimens in GT6 patients.

Systematic search of Pubmed and of major liver meeting abstract from 2015 and 2016 was performed. A total of 157 GT 6 subjects (with 6 subtypes) treated with SOF-based regimens from 7 Phase 2-4 studies were identified and included in this analysis. The analysis included treatment-naïve and treatment experienced subjects with HCV GT6 infection including subjects with cirrhosis and HCC but not posttransplant patients. Subjects received either SOF+ Peginterferon-α (PEG)/Ribavirin(RBV) for 12-24 weeks, SOF + RBV for 12-24 weeks, ledipasvir (LDV)/SOF for 8-12 weeks, SOF/velpatasvir (VEL) for 12 weeks. The 8-weeksLDV/SOF group only included patients without cirrhosis and without prior treatment failure.

Almost all (97%) were Asian with a mean age ranging from 49 to 58. One-quarter (38) had cirrhosis. The overall SVR12 rates ranged 95%-100% for all regimens including the 8-week treatment group. Serious adverse events (SAEs) were reported in 9%(1/11) of subjects in the SOF+ PEG/RBV arms, 0% in the SOF + RBV group, 3% (3/90) in the LDV/SOF group, and 2% (1/50) in the SOF + RBV group, 3% (3/90) in the LDV/SOF group, and 2% (1/50) in the SOF/VEL group. The most commonly reported AEs for SOF + RBV, LDV/SOF and SOF/VEL were fatigue, upper respiratory infection, and headache. In all 7 studies, there was just one subjects who discontinued due to an AE while receiving SOF + RBV.

This integrated analysis suggests SOF + PEG/RBV for 12-24 weeks, SOF + RBV for 12-24 weeks, LDV/SOF for 12 weeks, and SOF/VEL for 12 weeks all resulted in high cure rates among both treatment-naive and treatment experienced subjects with and without cirrhosis. SVR 12 rate was also high with only 8 weeks of LDV/SOF on patients without cirrhosis or prior treatment failure. Treatment completion was almost universal with all regimens, though significant AEs were common in regimens containing PEG and/or RBV.
Adverse events of HCV treatment using Sofosbuvir/Ledipasvir combination

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The incident of liver cancer in Mongolia generally caused by HBV and HCV, it is 7 times higher than that world’s average. In recent studies, 27% percent of the population has been diagnose and it is every 1 of 4 people has the virus and most prevalent cause of HCC and causing number one public health issue. Mongolia is one of the first countries that registered Sofosbuvir/ Ledipasvir (SOF/LDV) regimen from developing countries. The HCV treatment program in Mongolia has started on January of 2016.

Methods:
We followed and evaluated treatment outcomes of the patients with HCV infection using Harvoni (manufactured by Gilead Science). We started our prospective analysis on August until October 2016, for 3 months, on 1230 patients. All patients were treated with SOF/LDV for 12 weeks and, their treatment was evaluated by quantitative HCV-RNA assays prior and W (week) 4 and W12 of treatment. Sustained Virological Response (SVR) after 12 weeks of treatment was assessed. Virus genotype analysis using cDNA microarray, liver enzymes, CBC and drug related adverse events were assessed in every patient. All the tests were conducted at Happy Veritas Laboratories in Ulaanbaatar, Mongolia.

Results:
Total of 40 adverse events were observed in 527/1230 patients (43%). Single adverse events were observed in 358/527 (68%), whereas 2 events were observed in 116/527 (22%) and 3 or more events were observed 52/527 (10%) on patients respectively. Agewise 35 or lower aged patients were 43/153 (28%), age of 36 to 55, 295/655 (45%) and age of 56 of more, 190/422 (45%) were adverse evets were observed. Our result by gender wise, out of 406/781(52%) on female patients, on male patients, 121/449 (27%) were observed adverse events.

Conclusions:
Treatment of HCV in Mongolia using all-oral dual DAA was divided in 3 phases due to shortness of drugs and logistics arrangements. We were able to include only stage-one patients in this study. We have achieved 95.5% SVR12W for 3 months treatment with SOF/LDV this time. Despite the identical adverse events were found in other Asian and other regions in the world during treatment, unrecorded adverse were observed such as the facial paralysis, paraproctitis, AFP and facial skin darkening in Mongolia.

Efficacy and safety of Daclatasvir plus Asunaprevir treatment based on a real
Daclatasvir plus asunaprevir (DCV+ASV) treatment has demonstrated potent antiviral activity in patients with genotype 1b hepatitis C virus (HCV) infection. We investigated the real-world efficacy, changes in liver stiffness measurements and safety of DCV+ASV treatment in Korea.

A total of 306 patients with chronic hepatitis C were treated with DCV+ASV from August 2015 to July 2016. We excluded patients with resistance-associated substitutions (RAS) in NS5A and hepatocellular carcinoma at baseline. The patients received DCV (60mg once daily) plus ASV (100mg twice daily) for 24 weeks. Finally, 212 patients who were followed up for 12 weeks after the end of treatment were analyzed. We investigated virologic response and the changes of fibrosis with non-invasive markers before and after completion of the treatment.

The mean age was 60.8 years and female was predominant (63.2%). Treatment-naïve patients (61.8%) were in the majority and 44 (20.8%) patients had cirrhosis. 208 (98.1%) and 204 (96.2%) patients achieved end of treatment response and sustained virological response (SVR12), respectively. SVR12 rates were higher in patients who were less than 65 years old, male gender, those with cirrhosis and those with lower HCV RNA. Significant decline was observed in LS values, FIB-4 and APRI values between baseline and SVR12 regardless of presence of cirrhosis and treatment experience.

DCV+ASV dual therapy resulted in high SVR12 rates with improved liver fibrosis and the treatment was well tolerated in patients with genotype 1b HCV infection. Further studies are needed to monitor the longterm results of the DCV+ASV treatment.

Ledipasvir/Sofosbuvir single tablet regimen (Hepcinat-LP) highly effective

Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis. Moreover, it has the highest, and increasing rate of liver cancer and mortality due to liver cancer in the world. Cancer is the second most common cause of death in Mongolia and liver cancer is responsible for 44% of all cancers. Chronic hepatitis B and C infections are causes of 95% of liver cancers in the country. The aim of study is to evaluate treatment outcome of ledipasvir 90mg/ sofosbuvir 400mg (Hepcinat-LP, manufactured by NatcoPharma) in HCV patients with and without cirrhosis.
326 patients were treated. All the patients received a fixed-dose combination ledipasvir and sofosbuvir, administered orally once daily for 12 weeks or 24 weeks. The end points were the proportion of patients with sustained virological response 12 weeks after treatment, normalities of laboratory results and safety.

SVR12 rates were 98.77% (322/326). AST and ALT levels were significantly decreased and normalized within the first 4 weeks and remained stable until follow-up week 12 of treatment (P<0.001 and P<0.001, respectively). The most common adverse events were headache (14% of patients), fatigue (19%), and nausea (17%). No patients discontinued treatment because of an adverse event.

The combination of ledipasvir/sofosbuvir for 12 weeks produced high rates of SVR12 and well tolerated treatment in patients with and without liver cirrhosis.

Efficacy and safety of elbasvir/grazoprevir in treatment-naïve patients with HCV GT 1, GT 4 and GT 6 infection (C-CORAL): a phase III randomized multinational clinical trial

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Hepatitis C virus (HCV) contributes significantly to the overall liver disease burden in the Asia Pacific region and Russia. Seroprevalence rates vary from 1-5% and genotype (GT) 1b accounts for about 1/2 of infections. The efficacy and safety of the fixed-dose combination of elbasvir (EBR) 50 mg and grazoprevir (GZR) 100 mg has been demonstrated in a broad population of HCV-infected patients and supports evaluation in this region where clinical experience with direct-acting antivirals is limited. EBR/GZR is approved in the US and EU for treatment of HCV GT1 and 4 infection.

C-CORAL is a double-blind placebo-controlled, Phase 3 trial that randomized treatment-naïve HCV GT1, 4 or 6 infected patients in a 3:1 ratio to an immediate treatment group (ITG; 12 wks of EBR/GZR) or deferred treatment group (DTG; 12 wks of placebo, followed by 12 wks of EBR/GZR). Patients were enrolled in 2 cohorts: Cohort 1 enrolled 2 in mainland China. The primary endpoints include % of patients in the ITG who achieved SVR12 and a comparison of safety and tolerability of EBR/GZR in the ITG vs placebo in the DTG.

To date, data from Dohort 1 are available. In this cohort, a total of 250 patients were enrolled in the ITG and 86 in the DTG. Mean age (±SD) was 50±12 years, 57% were females, 59% were Asian, 74% were GT1b, and 19% were cirrhotic. SVR12 in the ITG was 92.8%. Eighteen subjects in the ITG did not achieve SVR12: 11 were relapses, 6 were on-treatment failures (all GT6) and 1 GT1b patient withdrew consent. The incidence of adverse events (AEs) was generally comparable between the ITG vs the DTG including drug-related AEs (21.2% vs 19.8%) and serious AEs (0.8% vs 1.2%; none considered drug-related). During treatment with EBR/GZR or placebo 2/250 (0.8%) patients in the ITG and 11/86 (12.8%) in the DTG had an
ALT value >5x ULN and greater than baseline. One patient in the ITG withdrew after meeting a trial specific discontinuation criterion for elevated ALT (not considered drug related). Updated safety and efficacy data will be presented for the ITG and DTG both cohorts.

A 12-week regimen of EBR/GZR is effective and well-tolerated in GT1 and GT4-infected, treatment-naïve patients in the Asia Pacific/Russia region.

Conclusions:

A 12-week regimen of EBR/GZR is effective and well-tolerated in GT1 and GT4-infected, treatment-naïve patients in the Asia Pacific/Russia region.


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The 2-DAA regimen of ombitasvir (OBV) and paritaprevir (identified by AbbVie and Enanta, with the pharmaco-kinetic (PK) enhancer ritonavir [RTV], PTV/r) + dasabuvir (DSV) has been approved for the treatment of HCV genotype (GT) 1-infected patients in many countries worldwide. ONYX-I (patients without cirrhosis) and ONYX-II (patients with compensated cirrhosis) are Phase 3 studies exploring the PK, safety, and efficacy of the 3-DAA ± ribavirin regimen in a HCV GT1-infected Asian population. Comparable PK exposures of the 3-DAA regimen between the Asian and predominantly Caucasian (thereafter referred to as “Western” HCV GT1-infected patients in other studies have been published.

We compared the safety and efficacy profiles of the 12 week 3-DAA regimen (+ ribavirin for patients with compensated cirrhosis) in Asian patients in ONYX-I and –II Phase 3 studies conducted in China, Taiwan, and South Korea with GT1b-infected Western patients enrolled in PEARL-II (treatment-experienced), PEARL-III (treatment-naïve), and TURQUOISE-II (compensated cirrhosis) Phase 3 studies conducted exclusively in North America, Europe, and Australia. Among treatment-naïve non-cirrhotic patients, sustained virologic response at post treatment week 12 (SVR12) was achieved by 99.5% (183/184; 95% CI 97.0-99.0) of Asian patients compared with 99.0% (207/209; 95% CI 97.7-100) of Western patients. In non-cirrhotic treatment-experienced patients, SVR12 was achieved by 100% (141/141; 95% CI 97.4-100) of Asian patients and 100% (91/91; 95% CI 95.9-100) of Western patients. Among cirrhotic patients, SVR12 was achieved by 100% (104/104; 95% CI 96.4-100) of Asian patients compared with 98.5% (67/68; 95% CI 95.2-100) of Western patients. The majority of Asian and Western patients with or without cirrhosis had at least 1 treatment-emergent adverse event (TEAE). Low percentages of Asian and Western patients (<4% in each study) experienced serious TEAEs. TEAEs leading to treatment discontinuation, in both Asian and Western patients, were rare. No patients without cirrhosis and 1 patient with cirrhosis discontinued treatment due to a TEAE. Only 1 death occurred across the studies, which was not due to TEAE.

The safety and efficacy profiles were consistent between the Asian and Western HCV GT1b-infected patients treated with OBV+PTV/r+DSV.
Effectiveness and safety of 3D (Paritaprevir/ Ritonavir and Ombitasvir in combination with Dasabuvir) therapy for treatment-naïve chronic HCV genotype 1b infection

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Objective: To evaluate the effectiveness and safety of the combination of paritaprevir /ritonavir /ombitasvir with dasabuvir (PTV/r/OBV+DSV) for 12 weeks in treatment-naïve chronic HCV genotype 1b infection.

Methods: Between Sep, 2015 and Apr, 2016, 10 treatment-naïve HCV genotype 1b-infected patients diagnosed at Tangdu Hospital received PTV/r/OBV+DSV for 12 weeks and followed up for 24 weeks. Sustained virological response at 12 weeks (SVR12) and 24 weeks (SVR24) after the end of treatment was assessed. Clinical and laboratory data, adverse events were reported.

Results: In 7 of 10 patients (70%), HCV-RNA levels decreased less than 15 IU/ml by 2 weeks of treatment. HCVRNA loads were undetectable and liver function was normal in all patients by 12 weeks of treatment. Furthermore, 10 patients (100%) achieved SVR12 and SVR24. The most common adverse events were asthenia and headache. No serious adverse events were observed.

Conclusions: The all-oral and interferon/ribavirin-free regimen of PTV/r/OBV+DSV for 12 weeks achieved 100% SVR12 and SVR24, improved liver function in treatment-naïve HCV genotype 1b-infected patients without cirrhosis. This regimen combination was well tolerated.
Liver fibrosis by Fibroscan in chronic hepatitis B patients during Tenofovir

Liver fibrosis and its sequel cirrhosis represent a major health care burden, and assessment of fibrosis by biopsy is gradually being replaced by noninvasive methods. In clinical practice, the determination of fibrosis stage is important, since patients with advanced fibrosis have faster progression to cirrhosis and antiviral therapy is indicated in these patients.

We aimed to assess the performances of liver fibrosis during antiviral treatment by liver stiffness (LS) measurement using Fibroscan in chronic hepatitis B (CHB) patients.

We followed and evaluated treatment outcome of fifty six patients with chronic hepatitis B, initiating their TDF regimen at Happy Veritas Clinic and Diagnostic Center. Each patient underwent transientelastography measurements, HBV quantification and serum liver marker assays before treatment with TDF, orally, once daily.

The mean age of the patients (27 men, 29 women) was 45±11. Before treatment LS measurement results indicated fibrosis stage F0 in 18 patients (32.1%), F1 in 6 (10.7%), F2 in 19 (33.9%), F3 in 18 (16.1%), and F4 in 4 patients (7.1%). After SVR12-SVR24 months the mean stiffness score of F1 increased from 7.8 to 8.3, F2 increased from 9.38 to 10.3, F3 decreased from 13.3 to 12.3, F4 increased from 23.8 to 28.4. In table 1 shows the changes of liver stiffness by Fibroscan after treatment.

Table 1. The changes of liver stiffness by Fibroscan after TDF treatment

<table>
<thead>
<tr>
<th>Liver fibrosis stage before treatment</th>
<th>F0</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>6</td>
<td>19</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>F0</td>
<td>16 (88.9%)</td>
<td>3 (50%)</td>
<td>4 (21.1%)</td>
<td>4 (22.2%)</td>
<td></td>
</tr>
<tr>
<td>F1</td>
<td>1 (16.7%)</td>
<td>1 (16.7%)</td>
<td>4 (21.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F2</td>
<td>1 (5.6%)</td>
<td>1 (16.7%)</td>
<td>4 (21.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
There was a significant negative correlation between platelet count and liver stiffness score.

In CHB patients who is receiving TDF regimen, annual LS measurement revealed that significant advanced fibrosis improvement slows but continues during treatment.

Efficacy of new direct acting antiviral therapy in treatment of cirrhotic and non-cirrhotic HCV Egyptian patients

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3Kafr Elsheikh Liver Research Center

Background: Egypt has the highest prevalence of hepatitis C virus (HCV) infection worldwide. Direct acting antivirals (DAAs) combination therapy make it is possible to eradicate HCV infection even in patients who were difficult to treat.

Objective: In the current study we aimed to assess the efficacy of different antiviral regimens allowed for treatment of cirrhotic HCV patients in Egypt.

Patients and Methods: 2632 chronic HCV patients who receive antiviral treatment were included. Of them 1091 were cirrhotic and 1541 were non cirrhotic. 2169 patients were treatment naïve and 463 patients were treatment experienced. The included patients received one of the following four regimens: (1) Interferon, Sofosbuvir and Ribavirin for 12 weeks (group I; n =618), (2) Sofosbuvir and Ribavirin for 24 weeks (group II; n =500), (3) Sofosbuvir and Simeprevir ± Ribavirin for 12 weeks (group III; n = 535) or (4) Sofosbuvir and Daclatasvir ± Ribavirin for 12 weeks (group IV; n = 979). The sustained virological response (SVR), HCV infection relapse, and treatment failure were assessed in all groups.

Results: The mean age of the included patients was 51.43 years; they were 1504 (57.15%) males and 1128 (42.85%) females. Among included patients (n = 2632) the overall SVR, HCV infection relapse and treatment failure were 92.1 % (n=2424), 6.3% (n=166) and 1.59% (n=42), respectively. The overall SVR, HCV infection relapse and treatment failure in cirrhotic patients were 87.26% (n=952), 11% (n=120) and 1.74% (n=19), respectively. Among the 4 regimens included, Sofosbuvir and Simeprevir ± Ribavirin had significantly higher efficacy in treatment of cirrhotic HCV Egyptian patients.

Conclusion: Direct acting antivirals have reasonable efficacy in treatment of chronic HCV Egyptian patients. Sofosbuvir and Simeprevir ± Ribavirin seems to be the most effective regimen in cirrhotic patients.
Health care workers in Mongolia: A nationwide survey

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1 Mongolian National University of Medical Sciences
2 Flagstaff International Relief Effort, USA
3 National Institutes of Health, USA

Background and objective: Health-care workers are at risk of infections associated with accidental exposure to blood, including viral hepatitis B (HBV) and C (HCV). Although there have been conducted several studies regarding HBV and HCV infection among health care workers, no nationwide survey was conducted thus far. We aimed to determine HBV and HCV infections and replication status among professionals working in all levels of healthcare organizations urban and rural areas of Mongolia.

Methods: A nationwide cross sectional survey was conducted with stratified multistage, random sampling from 4 geographical regions and capital city. A representative sample size was calculated. Serum samples were tested in the laboratory of National Institution for Health, USA. HBsAg, anti-HBc, anti-HCV, antiHIV were tested by ELISA, 3.0 Ortho Clinical Diagnostics whereas HBV DNA and HCV RNA detection and quantification were done by real time PCR method.

Results: Among 1020 healthcare workers 21.6%, 24.5% and 18.3% were enrolled from UB, province centers and soums, respectively. The seropositivity rates for anti-HBc, HBsAg, and anti-HCV were 68.2%, 7.6% and 21.9%, respectively. Doctors and nurses who were working in high risk departments had significantly higher rate of HBsAg (p<0.05) and anti-HCV (p<0.05) positivity compared to those working in low risk units. In addition, 0.7% were co-infected with HBV and HCV. Among HBsAg positive subjects 89.7% were positive for HBV DNA whereas 4.0% out of HBsAg negative but antiHBs positive subjects were positive for HBV DNA. HCV RNA was positive in 46.2% of anti-HCV positive participants.

Conclusions: Almost one third of healthcare workers had single or co-infection of HBV and HCV with significantly higher rate among professionals working in high risk units. High replication rates were observed among HBsAg and anti-HCV positive subjects.

Treatment efficacy of Lutasan injections on liver disorders

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2 Department of Gastroenterology, MNUMS
3 Department of Infectious Diseases, MNUMS

Chronic liver diseases are very common among the Mongolians. Study suggests that alcohol induced pathologies composed of cirrhosis 39%, fatty liver disease 27% and 11% chronic hepatitis respectively.
“Lutasan” (reduced glutathione) injection is known as hepatoprotector, antioxidant, immune modulator and detoxifying functions. As chronic disease progresses, glutathione insufficiency leads to poor cognitive outcomes and tremor in upper limbs. Therefore, we aimed to study treatment efficacy of “Lutasan” injection for chronic liver diseases and the complications.

Methods:
Total of ten subjects were recruited randomly from GI Department of Third General Hospital. Liver functions were evaluated by serum total bilirubin, total protein, albumin, AST, ALT, GGT, and alkaline phosphatase measures and hepatic neurocognitive deterioration was evaluated by Reitan neurophysiological test.

Results:
10% of the patients were alcohol induced, and 60% had combination of viral and alcoholic reasons, and remaining 20% had biliary tract disorders. Compare to the first day’s results, on the 10th day of hospitalization, serum indicators were much improved within the treatment period (*p <0.05) including AST 3.02 times, ALT 2.21 times, ALP 2.56 times and GGT 1.78 times were decreased respectively. (Table 1).

Table 1. Comparison of serum markers of liver functions on 10th day

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n=10</td>
<td>n=10</td>
</tr>
<tr>
<td>Total bilirubin (mcmol/l)</td>
<td>25.38±6.58</td>
<td>20.32±5.17</td>
</tr>
<tr>
<td>Total protein (g/l)</td>
<td>70.82±2.09</td>
<td>71.15±2.84</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>35.7±3.04</td>
<td>36.7±0.74</td>
</tr>
<tr>
<td>AST (GOT) (IU/L)</td>
<td>132.8±28.8</td>
<td>65.12±13.55*</td>
</tr>
<tr>
<td>ALT (GPT) (IU/L)</td>
<td>146.9±21.78</td>
<td>66.5±15.38*</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>272.8±13.1</td>
<td>106.61±13.63*</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>227.5±7.27</td>
<td>127.17±10.98*</td>
</tr>
</tbody>
</table>

Significance level: *p <0.05

Also neuro-cognitive improvements were significantly observed, by 1.74 times on Reitan neurophysiological test when comparing before and after treatment scores, 58.6±4.61 and 33.7±1.34, respectively.

These findings suggest that Lutasan, a glutathione supplement has effects of minimizing hepatic cytolysis, cholestasis in the biliary tract, reducing destruction of hepatocytes, and aiding regeneration of liver cells. Moreover, it reduces symptoms of hepatic neurocognitive disorders significantly.

Role of IL-28B genetic variants in HCV related liver disease severity in patients with different viral genotypes

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Background:
The role of host interleukin 28B (IL-28B) in liver disease severity in patients of chronic hepatitis C (CHC) is conflicting. Its impact on Asian patients with different viral genotypes remains elusive.

Objective:
To elucidate the effect of IL-28B genetic variants in a large Asian cohort with different viral genotype

Methods:
1288 biopsy proven CHC patients were enrolled for testing the association of liver fibrosis and IL-28B rs8099917 genotype

Results:
HCV genotype 1 (HCV-1) infection accounted for 59.4 % of the patients and the remaining 518 patients (40.6 %) were with HCV non-1 infection (the majority were with HCV-2 infection). Of the 1084 patients with IL-28 genotype available, nine hundred and twenty eight (85.6 %) patients were with TT genotype. Univariate analysis revealed that patients with advanced liver fibrosis (F34) were older, had lower platelet counts, high serum α-fetoprotein, alanine aminotransferase (AST) levels, had higher proportion of diabetes, and non-TT genotype carriage, APRI & FIB-4 level. Logistic regression analysis revealed that factors associated with advanced liver fibrosis included Age (odds ratio [OR]/95% confidence intervals: 1.023/1.009-1.037, p=0.001), diabetes (odds ratio [OR]/95% confidence intervals: 1.736/1.187-2.539, p=0.004), α-fetoprotein (odds ratio [OR]/95% confidence intervals: 1.007/1.002-1.012, p=0.009), platelet count (odds ratio [OR]/95% confidence intervals: 0.991/0.988-0.993, p<0.001), rs8099917 non-TT genotype carriage (odds ratio [OR]/95% confidence intervals: 0.585/0.400-0.856, p=0.006), While patients were divided based on their viral genotype. Factors independently associated with advanced liver fibrosis in patients with HCV-1 infection included diabetes (odds ratio [OR]/95% confidence intervals: 2.379/1.452-3.896, p<0.001), α-fetoprotein (odds ratio [OR]/95% confidence intervals: 1.023/1.012-1.035, p<0.001), platelet count (odds ratio [OR]/95% confidence intervals: 0.990/0.987-0.994, p<0.001), rs8099917 non-TT genotype carriage (odds ratio [OR]/95% confidence intervals: 0.529/0.328-0.854, p=0.009). On other hand, factors independently associated with advanced liver fibrosis in patients with HCV- non 1 infection included Age (odds ratio [OR]/95% confidence intervals: 1.039/1.016-1.063, p=0.001), platelet count (odds ratio [OR]/95% confidence intervals: 0.990/0.986-0.995, p<0.001).

Conclusions:
Unfavorable IL-28B genotype was associated with advanced liver disease. The genetic effect was restricted to patients with HCV-1 infection.

Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis.
We aimed to study efficacy of DAA treatment of ledipasvir/sofosbuvir (Harvoni) treatment among the target group of Arkhangai Province. To study improvement level of fibrosis among the patients with HCV using lab testing and imaging tests. To study treatment efficiency of DAA Harvoni among the HCV people.

The study was conducted at General Hospital of Arkhangai province commencing from 1 March, 2017 among the HCV patients who were receiving DAA Harvoni treatment within the framework of the project “Liver disease free Arkhangai”. The study is hospital based and cross sectional, with sampling of inclusion and exclusion criteria. In total 131 patients with age range of 28-66 years were involved. Mean age was 53.8±7.9, for men 45 and for women 86. Three patients were interferon treatment experienced. Several testing methods were used to define and compare treatment results between the periods of four weeks after commencement. They were HCV RNA viral load testing (Roche Molecular System, with min level is <15), blood analysis (WBC, HGB, PLT), Liver enzymes and others (Creatinine, T.bil, D.bil, ALT,AST,ALP,GGT,ALB, TP, glucose, AFP) and ultrasound images. Those results were analyzed to determine liver fibrosis level (APRI, FIB 4) and processed by Stata 12 software. The informed consent was introduced and signed.

Results:
8 of the total 131 participants were diagnosed as chirrosis and 123 of them had chronic hepatitis. There was not any complication of the patients with other chronic disease comorbidity. All the participants had 1B genotype HCV.
The most of the patients were HCV RNA 83.3% (n=109) negative at fourth week of the treatment and few of them had positive HCV RNA 16.7% (n=22) байв. (Figure1)
White blood cell level was reduced at fourth week from 5.9±1.7 to 5.6±1.5 and platelet was increased from 238.2±67.18 to 246±33.52. The fibrosis level was reduced at the fourth week of the treatment according to Api and Fib assessment.

Figure 1. HCV RNA result at 4th week of the treatment.

Liver fibrosis level was reduced by APRI and FIB4 assessment at 4th week of the treatment (P=0.003). Serum RNA negative results were 83.3% among the study participants at fourth week of the treatment. DAA treatment is effective at this stage among the study population and final conclusion will be done after SVR 12 result.

Efficacy and safety of sofosbuvir-based regimens for hepatitis C genotype 1 patients with moderately impaired renal function

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Treatment of chronic hepatitis C virus (HCV) infection in patients with chronic kidney disease (CKD) is essential. The availability of sofosbuvir (SOF) has dramatically improved overall HCV cure rates, however
there is insufficient data regarding its use in patients with CKD. We evaluated SOF in patients with hepatitis C genotype 1 (G1) and moderately impaired renal function.

Methods:

We retrospectively reviewed all patients treated with a SOF-based regimen from December 2013 through September 2015 at Virginia Mason Medical Center. Data was then collected for HCV G1 patients with CKD stage 3.

Results:

A total of 28 patients with HCV G1 and CKD stage 3 were treated with a SOF-based regimen. Twenty-one patients had CKD stage 3A (estimated glomerular filtration rate [eGFR] 45–60 mL/min/1.73m²) and 7 patients had CKD stage 3B (eGFR 30–45 mL/min/1.73m²). The overall rate of sustained virologic response 12 weeks after completion of therapy (SVR 12) was 85.7% (24/28). SVR 12 in CKD stage 3A patients was 81.0% (17/21) and in CKD stage 3B patients, SVR12 was 100% (7/7). Based on treatment regimen used, the SVR 12 was 81.8% (9/11), 92.3% (12/13), and 75.0% (3/4) for SOF/ledipasvir (LDV), SOF/simeprevir (SIM), and SOF/pegylated interferon (PEG)/ribavirin (RBV), respectively. Greater than 30% reduction eGFR was observed in 2 out of 21 patients with CKD stage 3A, and 2 out of 7 patients with CKD stage 3B.

Conclusions:

SOF-based regimens resulted in high SVR12 rates in patients with moderately impaired renal function. During therapy, HCV patients with CKD should be carefully monitored for worsening renal function.

Economic analysis of Daclatasvir plus Asunaprevir (DUAL) for the treatment of HCV genotype 1b in China

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⁵Bristol-Myers Squibb China, Shanghai, China

Chronic infection with hepatitis C virus (HCV) can lead to life-threatening and resource-intensive complications including decompensated cirrhosis and hepatocellular carcinoma. In China, HCV represents a significant burden, with an estimated viraemic population of 9,795,000. Current standard of care is pegylated interferon-alfa+ribavirin (PR), which has suboptimal efficacy and safety. Novel direct-acting antiviral (DAA) regimens have improved rates of sustained virologic response (SVR) and tolerability over PR. This study aimed to assess the economic outcomes of the DAA regimen daclatasvir+asunaprevir (DUAL) for patients with HCV genotype 1b from the Chinese payer perspective.

A published and validated chronic hepatitis C Markov model was used to perform a cost–utility analysis of 48 weeks PR (SVR: 62.4%, discontinuation: 3.9% [CCGenos study]; regimen cost: ¥47,760RMB) versus 24 weeks DUAL (SVR: 92.4%, discontinuation: 0.6% [AI447-114]) in treatment-naive patients with HCV genotype 1b. Sensitivity analyses were conducted to assess the drivers of cost-effectiveness and cost
thresholds at which DUAL is expected to be cost-saving. Model inputs (transition rates, health state costs and utilities) were derived from Asian-specific sources, where possible. Baseline characteristics were reflective of the China HCV population. A lifetime horizon was applied; costs and benefits were discounted at 5% annually.

DUAL was estimated to be dominant versus PR (with cost savings of ¥402) when priced at up to 178% the current price of PR. Cost offsets were driven by increased disease management costs for PR (¥55,337RMB versus ¥20,226RMB for DUAL), resulting from the decreased likelihood of SVR. Gains in QALYs and life years of 1.29 and 0.85, respectively, were estimated. Sensitivity analyses (Figure 1) demonstrated that key influencers were discount rate, time horizon and SVR. Threshold analyses demonstrated that, under alternative settings, DUAL could be priced up to 271% the cost of PR and remain dominant.

Downstream consequences of HCV infection are resource intensive. The prevalence of infection in China is considerable, and standard of care is suboptimal. In this context, the introduction of a cost-saving and clinically effective treatment option such as DUAL is likely to benefit both the Chinese population and payer. Figure 1. Univariate sensitivity and cost threshold analysis (CC: compensated cirrhosis)
The new era of HCV treatment came up thanks to those new drugs HCV infection became one of the curable diseases, and entire world is targeting free from HCV /WHO/. Therefore, there is need of to access milestones of diagnostic and treatment development of HCV in our country. Our study aim is to determine implementation of global trend for HCV diagnostic and treatment in Mongolia.

Methods:
This is qualitative study and we analyzed policy and strategic documents and statistics issued by Mongolian Government, Ministry of Health, National Insurance, National Center for Communicable Disease, Mongolian National University of Medical Sciences and other organizations.

Results:
Ministry of Health played very large role in introduction of new management of HCV into the country. It provided all the legal ground and support to service providers at all levels of care. New guideline was approved which includes all new schemes of the treatment, diagnostic methods, new drugs were registered, specialist doctors were trained and access of the new drug were widened thanks to joining the Access program from Gilead Sciences.

Government of Mongolia approved and started implementation of the National Programme “Wholesome Liver Mongolia” with purpose of reducing liver related diseases including viral hepatitis. The programme provides good support and contribution to activities directed to elimination of the viral hepatitis. Within the framework of the programme, viral load testing for the age group between 40 and 65 years old and partial drug cost will reimbursed from the Health Insurance Fund, which ease the access to diagnostics and treatment.

Conclusion:
All those achievements show that Mongolia has been able to introduce a comprehensive and efficient short-term treatment for HCV and free the population of that disease which may increase the mortality level due to liver cancer.

Ombitasvir (abt 267), ritanavir boost with dastasbuvir (abt 333) and prataspravir (abt 450) with or without ribavirin (RBV) in g1 special population in hemodialysis (HD) in chronic hepatitis C (HCV) patients. Drop C trial: an open label prospective clinical pilot study.
Primary objective:
To show the efficacy of the triple regimen (Paritaprevir, Ritonavir and Ombitasvir) by obtaining SVR12

Secondary objectives: Safety, tolerability

Thirty Six (36) patients (18 cirrhotics and 18 non-cirrhotics) were recruited from 4 dialysis centers across Brooklyn; in patients undergoing hemodialysis with chronic hepatitis C; genotype 1.

Demographics: Caucasians (2/36), Hispanic (6/36), African Asian (26/38), Asian (2/36)
Genotype: 1a (23/36), 1b (13/36)
IL28b: CC (9/36), CT (13/36), TT (14/36)
Metavir staging by Fibrosure: F0 (8/36), F1 (3/36), F2 (9/36), F3 (5/36), F4 (9/36)
The patients were divided into two groups: group A (n=18) with cirrhosis and group B (n=18) with no cirrhosis.

Group A: Ombitasvir (Abt 267) + Ritanavir + Datasbuvir (Abt 333) + Prataspravir (Abt 450); with 200 mg daily of RBV
Group B: Ombitasvir (Abt 267) + Ritanavir + Datasbuvir (Abt 333) + Prataspravir (Abt 450); without RBV.

Exclusion:
Decompensated Cirrhosis, Diabetic Retinopathy, Severe peripheral neuropathy, Cerebrovascular Accident, Severe Cardiovascular dysrhythmias, severe cardiomyopathy
Pulmonary embolism, pulmonary hypertension, pulmonary fibrosis and h/o repeated pulmonary edema. HIV, HBV, CMV, Dermatitis, Active drug and alcohol abuse, daily narcotic uses
Thrombocytopenia ≤ 90, 000, Hemoglobinopathies: Thalassemia major and minor, intermediate, sickle cell disease, HBSc, Heinz bodies. Autoimmune Hemolytic Antibody. Platelet antibodies quality/quantitative inherit platelet dysfunction. Major Depression. Malignancy, Undergoing chemotherapy, Severe electrolyte dysfunction, Lupus, dermatomyositis, Uncontrolled Psoriasis, Autoimmune Hepatitis, Chronic Pancreatitis.

Results:
Group A: At 12 weeks, SVR was 94.4% (17/18) and relapse rate was 11.1% (2/18) Group
B: At 12 weeks SVR was 94.4% (17/18) and relapse rate was 5.5% (1/18)

This study demonstrates a high SVR with a very short course DAA’s in HCV in patients on HD. Both the groups achieved overall 94.4 % SVR 12. Both groups had one patient with virological failure (5.5 %). A total of 3/36 (8.3%) patients relapsed; 2/18 (11.1%) in group A versus 1/18 (5.5%) in group B. Role of DAA’s in ESRD patients on HD in CHILD A cirrhotics have encouraging SVR rates; though carries a risk of higher relapse rate despite daily modified doses of RBV. Overall the drugs were well tolerated with minimal side events and without treatment failure. Triple therapy with RBV is a viable option and larger clinical trials will validate the efficacy and short treatment paradigm.
Chronic hepatitis B and C virus share common transmission pathways. Therefore, co-infection can be expected. The WHO estimates that worldwide 71 million people are infected with HCV and 250 million people are infected with HBV. Due to lack of large-scale population-based studies the exact number of HBV/HCV co-infected patients is unknown. In co-infected HBV/HCV patients, HBV replication is usually suppressed by HCV over the time.

We aimed to assess the virological reactivation of HBV after HCV treatment in patients with HBV/HCV coinfection.

In our study we used single center patient data. These patients are in treatment control of chronic hepatitis HBV/HCV co-infection in Happy Veritas Clinic and Diagnostic Center. From 369 HBV/HCV co-infected patients 84 patients are successfully finished their DAA therapy. In this study, we included 12 patients who had a HBV-DNA quantification results before and after DAA therapy.

The overall SVR_{6-12} rate was 100% of HCV patients. Before DAA therapy, virological reactivation of HBV was observed in three patients. However after DAA therapy HBV-DNA was not detectable in all three patients. For the patients previously HBV-DNA undetectable (HBsAg+), HBV virological reactivation was found in 5 (55.5%) out of the 9 patients. For the all patients after DAA therapy the clinical laboratory results were decreased due to normal range.

International studies show that HBV virological reactivation occurs after DAA therapy. From our study HBV virological reactivation observed 5 out of the 9 patients and reactivation was not so high (from 500 to 4000IU/ml).

For chronic hepatitis patients with current HBV infection, the risk of HBV virological reactivation is present and monitoring the HBV-DNA quantity level during therapy might be useful.

For patients with active HBV-DNA during DAA therapy further study should be done.
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ONYX-II is an ongoing Phase 3, open-label study of the 3 direct-acting antiviral (3-DAA) regimen of ombitasvir (OBV), paritaprevir (identified by AbbVei and Enanta) co-dosed with ritonavir (PTV/r) and dasabuvir (DSV) with ribavirin (RBV) in treatment-naive and treatment-experienced (interferon/pegylated interferon and RBV) patients with genotype 1b (GT1b) chronic hepatitis C virus (HCV) infection and compensated cirrhosis in China, South Korea and Taiwan. An analysis at post-treatment week 12 demonstrated a sustained virologic response at post-treatment week 12 (SVR12) rate of 100% and a favourable safety profile. The present analysis reports efficacy and safety results through post-treatment week 24 (SVR24).

 Patients with chronic GT1b HCV infection and compensated cirrhosis received OBV/PTV/r+ DSV + RBV for 12 weeks and will be followed for 48 weeks post-treatment. Efficacy was assessed by SVR12 and SVR24. Safety was assessed as the percentages of patients with treatment-emergent adverse events (TEAEs) and laboratory abnormalities. Safety and efficacy were assessed in all patients who received at least one dose of study drugs.

A total of 104 patients with chronic GT1b HCV infection (62% female, 100% Asian, 58% treatment-experienced) were enrolled from China (n=63), South Korea (n=21) and Taiwan (n=20). All patients received at least one dose of study drugs. The SVR24 rate was 100% (concordant with SVR12), with no patient relapsing between post-treatment weeks 12 and 24. Most TEAEs were mild in severity. The most common TEAEs (≥10%) were increased blood bilirubin unconjugated increased (12%), dizziness (11%) and fatigue (11%). Four patients had serious TEAEs and all were assessed as being possibly related to the 3-DAA regimen (one was assessed as being possibly related to RBV). One patient discontinued treatment due to TEAEs (elevations in alanine aminotransferase [ALT], aspartate aminotransferase [AST] and blood bilirubin) after 3 weeks of dosing but achieved SVR12 and SVR24 Laboratory abnormalities ≥ grade 3 were infrequent (ALT: 3%; AST2%; total bilirubin: 7%). No ≥ grade 3 haemoglobin decrease was reported.

SVR24 and SVR12 rates were 100% in HCV GT1b-infected Asian patients with compensated cirrhosis who were treated with OBV/PTV/r + DSV + RBV for 12 weeks. The regimen was generally well tolerated with mostly mild TEAEs reported.
Efficacy and safety of Ombitasvir/paritaprevir/ritonavir and dasabuvir in noncirrhotic Asian patients with genotype 1b chronic hepatitis C virus infection: ONYX-I post-treatment week 24 results

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Hepatitis C virus (HCV) genotype 1b (GT1b) is the most common genotype encountered in Asian patients with chronic HCV infection. ONYX-I is an ongoing phase 3, randomised, double-blind, placebo-controlled study of the 3 direct-acting antiviral (3-DAA) regimen of ombitasvir and paritaprevir (identified by AbbVie and Enanta, with the pharmacokinetic enhancer ritonavir) (OBV/PTV/r) and dasabuvir (DSV) in treatment-naive and treatment-experienced (IFN/pegIFN and ribavirin) non-cirrhotic patients with HCV GT1b infection in China, South Korea and Taiwan.

Methods

In this study, the safety and efficacy of OBV/PTV/r+DSV administered for 12 weeks were evaluated in non-cirrhotic Asian patients. Patients in Arm A received active study drug during a 12-week double-blind (DB) period, while patients in Arm B received placebo during the same period followed by an open-label (OL) period in which they received 12 weeks of active study drugs. Efficacy was assessed by sustained virologic response at post-treatment week 12 (SVR12) and week 23 (SVR24). Efficacy and safety results are presented for all patients who received at least one dose of active study drugs in the DB period.

Results

650 HCV GT1b patients (54% female, 100% Asian, 44% treatment-experienced) were enrolled from China (n=410), South Korea (n=120) and Taiwan (n=120), and randomised 1:1 to Arms A and B. In Arm A, SVR12 and SVR24 rates were 99.5% (183/184) in treatment-naive patients and 100% (141/141) in treatment-experienced patients. Most treatment-emergent adverse events (TEAEs) in Arm A patients were mild in severity, the most common (≥5%) TEAEs in Arm A were upper respiratory tract infection (10.5%), headache (6.2%) and dizziness (5.2%). Seven patients had serious AEs during active treatment (Arm A) and no Arm A patient discontinued treatment.

Conclusions

In non-cirrhotic Asian adults with HCV GT1b infection, treated with OBV/PTV/r+DSV for 12 weeks, SVR24 rates equaled previously reported SVR12 rated from this study (99.5% of treatment naive and 100% of treatment-experienced patients), and are consistent with other clinical trials with this drug combination. No patient experienced a relapse between post-treatment week 12 and 24. The treatment was generally well tolerated and with mostly mild TEAEs reported.

A study on genotype distribution and pre-existing DAA resistant polymorphisms of HCV GT1b in Mongolia


In the study, the genotype distribution and pre-existing DAA resistant polymorphisms of HCV GT1b in Mongolia were investigated. The results showed a high prevalence of specific polymorphisms that may affect the efficacy of DAA therapies.

Genotype 1b dominates (98.1-98.9%) among HCV detected in Mongolia [O.Baatarkhuu, 2006; Ts.Oyunsuren, 2010]. It has been described more than 50 resistant mutations and pre-existing polymorphisms of HCV genes affecting DAA-treatment success and they have been found in different populations with different frequencies: 0.3-100% [E.Poveda, et al. 2014; K.L.Bergar et al., 2014; A.Ahmed and D.J.Felmlee, 2015; S.Nitta, et al., 2016; S.Bagaglio, et al., 2016:]. However, the prevalence of pre-existing resistant polymorphisms of HCV in Mongolia, has not been studied, so far, except our previous in silico search for resistant mutations with 60 full HCV genomes detected in Mongolia stored in GenBank [S.Ganchimeg et al., 2015].

We have started since January of 2016 use HCV Genotype Array TestVer.2 Kit (DiagCorGenFlow, HK) which enables to detect all HCV genotypes and Q80K polymorphisms. In this report, we have analyzed 211 patients who approached “Gyals” Medical Center, LLC, Ulaanbaatar for HCV genotypes and Q80 polymorphisms test.

HCV genotype 1b was detected in 210(99.5%) of all tested subjects. Among HCV genotype 1b infected subjects there were two cases were co-infected with genotype 2, one case was co-infected with genotype 3 and one case was co-infected with genotype 6. Also, HCV genotype 3 was detected from only one subject. Results have showed that Q80 mutation was found in 109(52%), Q80K mutation was found in 15(7%) and 86(41%) showed non-Q80K or Q80(X) mutation.

Q80K, Q80L, Q80N, Q80R, Q80H mutations detected on the NS3 gene of HCV genotype 1a increases the virologic failure rate of treatment outcomes with DAA-based regimens which targets NS3 gene and Q80(X) mutations coexists with other mutations on NS3 gene folds the resistance rate [N.Mani et al., 2012; T.Kanda et al., 2014]. In Americas, Q80K mutation were found in 40% among HCV 1a genotype infected individuals [P.Kwo et al., 2016]. Overall, Q80K mutation was 30% in subjects infected with HCV genotype 1a and 0.5% in subjects infected with HCV genotype 1b [L.Izquierdo et al., 2014; O.Lenz et al., 2015]. Therefore, WHO recommends to screen NS3 Q80K polymorphism prior prescribing simeprevir [WHO, 2016:].

12 among 110 Q80 genotype subjects were tested their HCV viral load and had DAA treatment with Ledipasvir/Sofosbuvir (Harvoni) whereas 8 among 86 non-Q80K wild type at our medical center. SVR of these individuals were 100% regardless of polymorphism.

The association between steroid hormone and hepatitis C virus genotype 1

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Hepatitis C virus, an important risk of liver cirrhosis and hepatocellular carcinoma, is the major healthcare problem worldwide. The standard antiviral treatment by interferon and ribavirin has been the standard of care, however, the response in males and females showed the different efficacy. Hence, it is important to identify the role of steroid hormone in HCV antiviral therapy.

HCV NS 3 and NS 5A were determined in HCV genotype 1 replication cell lines, and also in infected cells by androgen and estrogen combined with antiviral treatment in steroid-starved culture conditions. A cohort statistical data of viral loads was analyzed in HCV genotype 1 male and female patients.

When combined with steroid hormone in antiviral treatment, the HCV NS 3 and NS 5A protein expression level were showed in inversed phenomena. Androgen would enhance the viral protein expression level in Ava 5 and Con 1 cells, also in infected HCV genotype 2a cells, but opposite affect shown by estrogen in steroid-reduced conditions. The similar phenomena were observed in the cohort study.

Our results showed that steroid hormone may affect the HCV viral protein expression that might explain the different progression of HCV in different gender. A better understanding the affecting action of steroid hormone in antiviral treatment could be beneficial in developing novel therapeutic regimen.

Elevated Interleukin 4 level predicted advanced fibrosis in chronic hepatitis C

Cytokine imbalance had been associated with chronic hepatitis C virus (HCV) infection. This study was aimed to investigate the relationship between interleukin 4 (IL4) and development of liver fibrosis in chronic hepatitis C (CHC) patients.

Ninety two liver biopsy proven CHC patients were enrolled in this study. Demographic features and biochemical analyses were collected and fluorescent Bead immunoassay was used to measure cytokine levelof the serum IL4. The multivariate logistic regression test was further performed to identify the
independent factors to predict liver fibrosis. The area under curve (AUC) was calculated using receiver operating characteristics (ROC) analysis. The optimum cut-off value of IL4 concentration to divide the risk strata was calculated by the Youden index.

Of the 92 HCV infected patients, 23 (25%) patients had advanced (fibrosis grade 3-4) fibrosis. By univariate analysis, advanced fibrosis group patients had higher IL4 level (mean±SE of 309.6±41.5 vs. 527.6±99.7 pg/ml, p=0.019), older age (mean±SD of 56.3±7.4 vs. 50.4±9.7 years, p=0.009), high GOT level (mean±SD of 120.8±63.2 vs. 92.4±55.5 U/l, p=0.048), high Ferritin level (mean±SD of 641.0±548.0 vs. 384.1±363.6 ng/ml, p=0.013) and lower Platelet level (mean±SD of 153.2±48.5 vs. 184.5±61.6 10^9/l, p=0.030) compared to the mild fibrosis group. The accuracy of discriminating advanced or mild liver fibrosis was acceptable when IL4 cut-off level was set at 490pg/ml and the AUC was 0.659 (95% Confidence Interval [CI]=0.5120.806, p=0.041). Patients with higher IL4 concentrations (≥490 pg/ml) had more likely to have advanced fibrosis (57.9% vs. 31.5%, p=0.042) than lower IL4 concentrations. The multivariate analysis revealed that baseline IL4 level was an independent factor for predicting advanced fibrosis (adjusted Odds Ratio=4.26, 95%CI=1.13-16.02, p=0.032). IL4 level was significantly different in advanced and mild fibrosis groups with HCV genotype 1 (706.8±519.5 pg/ml vs. 285.1±303.3 pg/ml, p=0.007) compared to HCV genotype non 1 group.

Conclusion:

Our findings suggest elevated IL4 level predicts advanced fibrosis in CHC patients. The prediction effect was restricted to patients with HCV genotype 1.

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**Occult hepatitis B virus persistence in liver transplant recipients despite prophylactic hepatitis B immune globulin and potent nucleos/tide analogues therapy**

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Recent reports advocate for the complete withdrawal of HBV prophylaxis from liver transplant (LT) recipients with a low risk of HBV recurrence (ie. Undetectable serum HBV DNA). However, occult HBV persistence, particularly in extrahepatic tissues (ie. lymphoid system), remains a potential concern in LT recipients. In plasma and peripheral blood mononuclear cells (PBMC) of LT recipients, we aim to 1. Determine if HBV genomes and replication persists despite use of potent anti-HBV therapies and 2. Determine if HBV oncogenic genotypes and genetic variants are present.

Plasma and PBMC were collected from LT recipients (n = 12; 10 males; median age = 57.5; median followup most-LT = 60 months; 6 with pre-LT hepatocellular carcinoma [HCC]). All cases were treated post-LT with HBIG, NAs, and immunosuppresive. 3 cases have clinically detectable HBV DNA (lower limit = 10 IU/ml) and were HBsAg + post-LT. HBV DNA was detected by nested PCR using HBV specific primers. Next generation sequencing (NGS) of the PCR amplicons with Illumina MiSeq was used to identify HBV genotype and genetic variants. HBV covalently closed circular DNA (cccDNA) was detected in PBMCs (following Hirt total DNA isolation, T5 exonuclease digestion) with cccDNA primers specific dor the HBV nick region. PCR amplified
sequences were confirmed by nucleic acid hybridization to a Digoxigenin-labeled HBV specific probe and direct sequencing. HBV mRNA was extracted from PBMC and detected with reverse-transcriptase nested PCR.

HBV DNA was detected using nested PCR in both plasma and PBMC in all LT recipients. HBV cccDNA and mRNA were detected in the PBMC 5/12 and 2/12 cases, respectively. NGS analysis showed significant diversity in HBV quasi-species population size (i.e. 143-2212 non-redundant representative sequences) in plasma and PBMC. In all cases, single nucleotide polymorphisms previously reported to be associated with HCC were detected at varying frequencies.

Both chronic (HBsAg+) and occult HBV infection persists long term in the plasma and PBMC of LT recipients despite potent HBV prophylaxis as demonstrated by detection of HBV DNA, cccDNA, and mRNA. Further, genetic variants associated with HCC are present in the plasma and PBMC of cases with pre-LT HCC. Occult HBV persistence post-LT with oncogenic quasi-species suggest that extreme caution or close monitoring is necessary if complete withdrawal of HBV prophylaxis is attempted in LT recipients with a history of HBV-related end-stage liver disease.

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Hepatitis C virus (HCV) infection is one of the major causes of chronic hepatitis and hepatocellular carcinoma (HCC) around the globe. The prevalence of the HCV infections prevalence among children is not prevalent. The objective of the study was investigated to determine the prevalence of anti-HCV antibodies among school children in certain districts of Ulaanbaatar.

This is a cross-sectional study conducted among 10-15 school-aged children. The study participants were selected according to the randomized sampling procedure in the Sukhbaatar, Chingeltei, Bayanzurkh districts of Ulaanbaatar. A Lab test for anti-HCV was performed using HISCL 5000 analyzer SYSMEX Corp. Japan and study was funded by the SYSMEX Corp. Japan, Tottori University of Japan and Mongolian National University of Medical Sciences (MNUMS).

A total of 452 children were randomly selected (186 boys and 266 girls; age range 10-15 years). In the Sukhbaatar district, they were 42 boys and 60 girls, in Chingeltei district there were 45 boys and 72 girls, and in Bayanzurkh district there were 99 boys and 134 girls. Among study participants, 33.6% live in apartment and the rest were residing in house and ger district. According to the estimation of the family members, mean is 4.7 (min=4.6; max=4.8). In a total, three subject was confirmed to be an anti-HCV seropositive, estimating the prevalence of 0.6%, all of whom were girls.

The prevalence of anti-HCV seropositivity was 0.6% among children aged 10-15 years in some districts of Ulaanbaatar.
Prevalence and risk factors for hepatitis B infection in the adult population of Georgia: a nationwide survey

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Background and objective: This abstract presents the prevalence and risk factors of hepatitis B virus (HBV) infection based on a nationally representative survey of hepatitis B and C, conducted in 2015.

Methods: A cross-sectional, nationwide survey among general population aged ≥18 years (n=7,000) was conducted using a stratified, multi-stage cluster design with random sampling. Trained data collection teams collected demographic data, medical and behavioral history, risk factors and knowledge about HBV and obtained a blood samples, which were tested for anti-HBc antibodies, and anti-HBc+ samples were screened on HBsAg. Both tests were performed by ELISA. Prevalence of anti-HBc and HBsAg, and bivariate associations between anti-HBc and potential exposures were calculated.

Results: Prevalence of hepatitis B surface antigen (HBsAg) was 2.9%: 3.4% (95% CI=2.48-4.34) in males and 2.5% (95% CI=1.92-3.15) in females. There was no statistically significant difference between urban vs. rural residence (3.1% vs. 2.8%). HBsAg prevalence in Tbilisi (capital) was lower (2.3%) compared to three other major cities (5.1% in Batumi, 5.3% in Kutaisi, 5.2% in Rustavi). Prevalence of anti-HBc was 25.5% nationally. Bivariate analyses revealed significant associations between anti-HBc+ status and history of blood transfusion (OR = 1.9, 95% CI=1.48-2.37), dialysis (OR =4.0, 95% CI=1.08-14.53), injection drug use (IDU) (OR 2.8, CI 1.91-4.09), at least one invasive medical procedure (OR = 1.2, 95% CI=1.05-1.47) and incarceration (OR=1.9, 95% CI=1.32-2.86).

Conclusions: Prevalence of chronic hepatitis B is almost similar to the prevalence in Middle East and the Indian subcontinent (2-5%). The high prevalence of anti-HBc among persons with a history of blood transfusion, dialysis, IDU, invasive medical procedures, and incarceration could indicate that transmission occurs through these exposures, and provides guidance for groups where further efforts to improve education, prevention, and safe injection and blood programs could be concentrated. High prevalence in other major cities compared to the capital indicates the need to strengthen regulations and infection control in these areas. Hepatitis B vaccine has been included in the national immunization schedule since 2002, and coverage among children reached 93.7%. High anti-HBc prevalence among adults indicates that vaccination should be expanded to adults as part of Georgia’s HBV prevention efforts.
Advancing age and comorbidities in chronic hepatitis B patient result of 10 year longitudinal analysis of a diverse population-based cohort of 44,026 chronic

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The prevalence and impact of advancing age of and co-morbid medical condition among patient with chronic hepatitis B (CHB) poorly understood. Our goal is to examine the prevalence of co-morbidities in large diverse CHB population and temporal changes over the past 10 years.

The study identified CHB patients ≥ 18 years of age without hepatitis delta co-infection (ICD-9 diagnosis codes 0.70.22, 0.70.30 or 0.70.32) who were continuously enrolled for 6 months before and after CHB diagnosed from the 7/1/2004 to 6/30/2015 MarketScan Commercial (general population), Medicare (mostly over 65 years of age) and Medicaid (low income population) databases.

We included 44,026 CHB patients: 29,585 Commercial (median age 47 in 2006, 51 in 2015), 2,938 Medicare (median age 71 in 2006, 73 in 2016) and 11,503 Medicaid (median age 45 in 2006, 52 in 2015) patients. Deyo-Charlson Comorbidity Index scores increased over time for all payers with the largest increase in Medicare (1.6 in 2006 to 3.2 in 2015). The proportion of CHB patients with diabetes hypertension and hyperlipidemia increased significantly (all p<0.001) between 2006 and 2015 for all payers (Figure). Notable from 2006 to 2015, hyperlipidemia increased from 8.4% to 47.3% and hypertension from 43.0% to 75.9% for Medicare, Furthermore, the prevalence of non-alcoholic fatty liver disease (NAFLD) and hepatic steatosis increased by almost 4 folds for Commercial (1.6% in 2006 to 5.7% in 2015) and over 2 folds for Medicaid (1.8% in 2006 to 4.5% in 2015) (p<0.001). Glomerulonephritis, proteinuria, nephrotic syndrome or nephropathy prevalence also increased significantly for all payers by 2 to 4-folds from 2006 to 2015 (p<0.001):4.5% to 8.0% in Commercial, 11.6% to 43.7% in Medicare, and 9.5% to 20.2% in Medicaid. Liver and Renal impairment also increasingly affect CHB patient in all payer groups: one-third of Medicare (34.7%) and Medicaid (32.8%) and close one to one-fifth of Commercial (15.5%) patients by 2015.

Between 2006 and 2015, the median age of patients with CHB increased in the United States across payer types, and the proportion of patient with comorbidities also increased significantly across payers, up to 4-fold, and affected up to one-third of the CHB population. Advancing age and associated comorbidity profiles of CHB patient should be considered in management of these patient.
Prevalence of hepatitis B and hepatitis C virus infections among nurses in a tertiary hospital in Mongolia

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M. Colombo, W. Lange studies showed that 30-40% of people became chronic after suffering from Hepatitis B and C virus, about 50% of chronic cases transformed into primary liver cancer. There are few studies in our country were conducted on hepatitis among healthcare professionals, particular nursing personnel. The study was conducted to identify of hepatitis B and C virus among nurses and make recommendations to prevent and control of Hepatitis B virus and Hepatitis C virus.

Methods:
We carried out cross-sectional study among selected nurses, to determine surface antigen of hepatitis B virus and antibodies to hepatitis C virus. For identification of these antibodies and antigen, and validation of results Elisa tests from CTK Biotech Company (USA) and simplifying diagnostics were used.

Results:
There were 598 nurses from the First Central Hospital, the Second Central Hospital, the Third Central Hospital, Hospital of Ministry of Justice and Internal Affairs, and the National Center of Maternal and Child Health who participated in the study. From 5 hospitals 598 nurses surveyed and revealed the hepatitis B virus surface antigen positive 18.9%, hepatitis C virus antibodies in 23.1%, B and C viruses detected by 1.2% combined. There is an urgent need to provide knowledge to medical personnel regarding standards during procedures, concerning hepatitis infections, monitoring and improve technology used during procedures.

Conclusions:
The study identified that 43.2 percent of nurses surveyed on hepatitis B and C viruses were detected; it shows a high prevalence among the nurses.

Prolonged RNA interference therapy with ARC-520 Injection in treatment naïve, HBeAg positive and negative patients with chronic HBV results in significant

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Background and objective: ARC-520 Injection (ARC), a RNA interference drug, targets cccDNA-derived mRNA in chronic hepatitis B patients (CHB). We previously reported safety and antiviral activity of single, ascending doses of ARC in CHB. Here we report the HBsAg reduction and safety in multi-dose extension.

Methods: 8 CHB (5 HBeAg-neg, 3 HBeAg-pos) received up to 12 doses of 4 mg/kg ARC once every 4 weeks with daily entecavir (ETV). Naïve CHB who previously received a single IV dose of 4 mg/kg ARC and started daily ETV on the same day were eligible. Viral DNA and antigen knockdown (KD) were measured at regular intervals [qHBsAg, HB core-related antigen (qHBcrAg) in all, q HBeAg in HBeAg-pos].

Results: Patients received ETV for 34 to 44 weeks after a single dose of ARC before receiving the first ARC dose of the multi-dose extension. All CHB had viral DNA undetectable throughout the extension. After a single dose of ARC, qHBsAg in 3 of 3 HBeAg-pos and 1 of 5 HbeAg-neg remained below baseline. Multi-dose re-challenge resulted in additional qHBsAg KD in all CHB. Two distinct patterns of qHBsAg KD were seen: an immediate, direct ARC antiviral effect in all HBeAg-pos and a delayed response in all HBeAg-neg. In HBeAg-pos max reduction was 1.6 log (mean max 1.5) for qHBsAg after a single dose and 2.9 log (mean max 2.1) after multiple doses. In HBeAg-neg max reduction was 0.5 log (mean max 0.4) for qHBsAg after a single dose and 1.2 log (mean max 0.7) after a multiple doses. qHBcrAg and qHBsAg results are pending. ARC was well tolerated -50% reported a mild adverse event (AE) with no AE rated serious, severe, or causing withdrawal. The most frequent AEs were fever and malaise, consistent with mild infusion reactions.

Conclusions: (1) ARC was well tolerated when dosed every 4 weeks. (2) ARC + ETV suppressed HBV DNA to undetectable levels. (3) A single dose of ARC together with ETV resulted in reduction of HBsAg up to 44 weeks. (4) Multiple doses of ARC resulted in an additional reduction in HBsAg in all CHB. (5) HBeAg-pos CHB showed a larger, multi-log reduction in HBsAg, while HBeAg-neg CHB showed a lower reduction with delayed onset. (6) This is consistent with previous findings in chimps showing more cccDNA-driven antigen production in naïve HBeAg-pos and a higher fraction of qHBsAg from integrated DNA in HBeAg-neg. (7) Delayed onset of HBsAg reduction in HBeAg-neg CHB may be an indirect effect of KD of other viral proteins.

Serum wisteria floribunda agglutinin positive Mac-2-binding protein predict significant fibrosis in patients with chronic hepatitis B

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Wisteria floribunda agglutinin positive Mac-2-binding protein (WFA⁺-M2BP) was a novel serological marker of liver fibrosis. We aimed to investigate serum WFA⁺-M2BP level in the prediction of liver fibrosis in subjects of hepatitis B virus (HBV) infection and also to develop a predictive model for significant fibrosis.
A total of 160 patients, who were diagnosed with chronic HBV infection and received liver core biopsy prior to antiviral therapy during 2000 and 2015, were recruited. The liver biochemistry, HBV serological markers, and viral load were tested at enrollment. The aspartate aminotransferase (AST)-to-platelet (PLT) ratio (APRI) index and Fibrosis-4 (FIB-4) index were calculated. Serum WFA'-M2BP level was quantified and further indexed using the common equation. The grade of necroinflammation and stage of fibrosis were determined according to the METAVIR scoring system.

Results:
Of all, 123 (76.9%) patients were male and the median age was 40 years. One-third of the patients had positive HBeAg with a median HBV DNA level of 5.9 log_{10} IU/ml. The median WFA'-M2BP level, APRI and FIB-4 index were 1.20 COI, 1.19 and 1.63. Significant fibrosis (≥ F2) was found in 88 (55%) of the 160 patients. Serum WFA'-M2BP level was significantly associated with age, PLT, AST, APRI, and FIB-4 index. There was a significant difference of WFA'-M2BP level between groups of necroinflammation and fibrosis. The Areas under the receiver operating characteristic curve (AUROC) of WFA'-M2BP level for predicting fibrosis stages were 0.780 (≥F2), 0.785 (≥F3), and 0.769 (≥F4) (all p <0.001). The optimal cutoff value of 1.345 was identified to predict significant fibrosis with the sensitivity, specificity, PPV, NPV and accuracy of 65.9%, 80.6%, 80.6%, 65.9% and 72.5%. The multivariate analysis also identified serum WFA'-M2BP level as an independent factor associated with significant fibrosis (OR 3.0, 95% CI 1.73 - 5.31, p <0.001). Serum WFA'-M2BP combined with PLT achieved a high specificity and PPV of 91.7% and 89.3%. Patients with both serum WFA'-M2BP level ≥1.345 and PLT level <215 x 10^3/μl were at a significantly higher risk to have significant fibrosis comparing to patients with none of the parameters. (OR 17.4, 95% CI 5.74 - 52.90, p <0.001)

Conclusion:
Serum WFA'-M2BP level significantly predicts liver fibrosis in patients with chronic HBV infection. The combination of serum WFA'-M2BP and PLT level accurately identified patients with significant fibrosis, which helped in the decision making of antiviral therapy.

Epidemiological and clinical features of acute viral hepatitis B

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To study the epidemiological and clinical characteristics of acute viral hepatitis B in 2015-2016 reports, NCCD

It is a descriptive study. Among 100 patients diagnosed with acute hepatitis B virus infection, had clinical symptoms, serum ALT>500IU/ml, HBsAg positive and visited during 2015 to 2016 in National Center for Communicable Diseases.

100 patients (aged 24.05±4.5, 55 male and 45 female) with acute viral hepatitis B. Out of these 23% were student, 56% were employment and 21% were unemployment. From the epidemiological anamnesis dental treatment in 16.25%, tattoo in 11.8%, admitted hospital in 40%, surgery in 14.4% and blood transfusion in 4.4%
Common symptoms were fatigue (74.4%), loss appetite (81.25%), fever (23.75%), insomnia (15.6%), arthralgia (33.3%), epigastric pain (82.5%), vomiting (75%) and headache (30.6%).

Blood test results showed Total bilirubin 136.9±64.8, ALT 2594.2±1504.4, AST 1506.9 ±1273.7, Total protein 66.5±6.1, ALP 207.3±63.8 and Platelet 221±69.5 in the beginning of the symptoms. Serological test result had showed HBsAg positive in 87.8%, HBeAg positive in 8% and anti-HBc positive 51%. After 6 months from beginning symptoms repeated serological test were HBsAg negative in 87.8%, anti-HBs positive in 27.3%, anti-HBc IgM positive in 45.5% and anti-HBe positive in 36.4%.

Improved bone and renal safety of switching from tenofovir disoproxil fumarate to tenofovir alafenamide: preliminary results from 2 phase 3 studies in HBeAg positive patients

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Treatment with tenofovir alafenamide (TAF) has shown less bone and renal effects with similar efficacy rates compared to tenofovir disoproxil fumarate (TDF) in two large multinational Phase 3 studies after 48 weeks of therapy. Here, we evaluate patients who have completed 96 weeks of double blind treatment with TAF of TDF and have switched to open label treatment with TAF to determine changes in bone mineral density, creatinine clearance, and the maintenance of viral suppression.
A total of 540 subjects had entered the OL TAF phase after 96 weeks of blinded therapy across both studies. Creatinine clearance improved significantly in patients switched from DB TDF to OLTAF at Week 120 compared to Week 96 (N = 117, mean (SD) change = +2.43 (12.81) ml/min, p = 0.04); and remained stable in those previously receiving TAF. BMD also showed improvement at Week 120 from Week 96 among patients switched from DB TDF to OLTAF (hip: N= 58, mean (SD) % change = +0.71% (1.43), p = 0.0004; spine: N = 60, mean (SD) % change= +1.41% (2.30),p < 0.0001). BMD changes in hip and spine for DB TAF patients entering the OL TAF period were relatively stable. Compared to results at Week 96, high rates of virologic control were maintained across subjects in both studies during the OL period (97-99% and 80-83% in Studies 0108 and 0110, respectively).

Patients who switched from TDF TAF treatment demonstrated rapid improvements in DMB and creatinine clearance within the first 24 weeks of treatment, and virologic control was maintained. Longer term data is required to establish the benefits of switching to TAF for treatment of CHB.

Decrease in liver stiffness due to HCV treatment measured by transient elastography in Mongolian population

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The prevalence of liver cancer in Mongolia is 7 times higher than that of world average, generally caused by HBV and HCV. The most prevalent cause of HCC in Mongolia, HCV, accompanied with liver stiffness and cirrhosis, is an emerging public health issue. Mongolia is one of the first countries that registered Ledipasvir/Sofosbuvir (LDV/SOF) regimen from developing countries. By the support of Access program run by Gilead Sciences, USA, we started HCV treatment program from January 2016.

We followed and evaluated treatment outcome of patients with HCV infection using combination of 90mg ledispavir/400mg sofosbuvir (manufactured by Gilead Science) in 298 treatment naïve patients. All patients were treated with LDV/SOF for 12 weeks and, their treatment was evaluated by quantitative HCV-RNA assays prior and W (week) 4 and W12 of treatment. Sustained virological response (SVR) after 12 weeks treatment was assessed. Virus genotype analysis using cDNA microarray, liver enzymes, CBC and drug related adverse events were assessed in every patient. The laboratory tests were conducted at National Center of Communicable Diseases and Happy Veritas Laboratories.
Out of 298 patients underwent treatment, 138 patients were examined for pre-treatment liver stiffness using Fibroscan. When patients were examined by Fibroscan test, 25% (n=35) of assessed patients were F0 stage; 13,57% (n=19) were F1 stage; 10% (n=14) were F2 stage; 20,71% (n=29) were F3 stage; and 30,72% (n=43) were F4 stage. Patients (n=35) with fibrosis stage F0 were omitted from post-treatment control examinations. The one hundred three patients were selected for further post-treatment fibrosis staging. The twenty three patients were successfully contacted and complied post-treatment Fibroscan scanning. 23/23 (100%) patients achieved SVR12W, were all genotype 1b. Median ALT level significantly dropped during treatment from 121,19±98,3 IU/L to 33,2±14.7 IU/L and slightly increased by the end of treatment 41,4±18,8IU/L. The ninety one percent of the patients had improved in liver stiffness while remaining patients were observed increased stiffness.

After treatment, 30,43% (n=7) of patients moved to the F0 stage from liver stiffness. There are many studies that assess liver fibrosis after cure of HCV, but varying numbers were observed. We assess liver stiffness after treatment of HCV in Mongolian population for the first time. Though study population was small, we had 91% of patients improved in liver stiffness. Better compliance, active doctor’s participation is needed in further studies.

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**Immunization capacity of HBV vaccination and immunization after HBV infection**

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As of 2015 over 257 million people live with chronic Hepatitis B virus infection in the world. Every year about 887,000 people died due to liver cirrhosis or liver cancer caused by Hepatitis B virus. HBV and HCV are high prevalent in Mongolia, around one fourth Mongolian has HBV or HCV. According to the study, 39.4 percent of people who had HBV infection got HBV vaccination which leads to vital problem in Mongolian health care system. Since 1991 all newborns have been vaccinated with HBV vaccine. And people who born before that year did not take the HBV vaccination.

We aimed to determine the generation of persistent immunity from HBV vaccination or after infecting with HBV infection.

492 patients have enrolled who were investigated with quantitative HBsAb (qHBsAb) using Sysmex HISCL - 800 (full automated analyzer) at Happy Veritas Diagnostic and Treatment Center. The vaccination scheme consists of three doses. Vaccination is successful if the antibody-titer (qHBsAb) is higher than 10 mIU/L. Also we have conducted questionnaires about HBV vaccination and risk factor for taking Hepatitis infections from patients.

In this study 492 patients have participated, 313 female (63%) and 179 male (37%), out of which 471 (96%) people born before 1991 and remaining 21 (4%) people born after 1991. Twelve people (57%) who born
after 1991 or vaccinated within 24 hours after birth were qHBsAb low titer (<10 mIU/L), remaining (43%) were qHBsAb titer (>10 mIU/L), while 297 people (64%) who born before 1991 were qHBsAb titer (<10 mIU/L), and remaining 36% of patients had persistent HBV vaccine. The 99 people who born before 1991 have enrolled in HBV vaccination voluntarily while 372 people did not take HBV vaccine at all.

Persistent immunity against HBV is generated not only in person who have taken HBV vaccination but also in person who have had slight HBV infection.

It was considered that people aged between 50 and 60 years could not get persistent immunity against HBV. We assumed that persistent immunity against HBV depends on age, not other factor and sex.

Sero-prevalence of Hepatitis C virus and risk factors for HCV study among 40-65

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Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis.

We aimed to determine HCV seroprevalence and risk factors for hepatitis C among 40-65 aged population of Arkhangai province.

The survey is conducted by randomly cross-sectional design of a descriptive study, selected target group of 17600 people, and from 21700 people aged 40-65 in Arkhangai province. We randomly chose 464 participants from 7 soums /from 19 soums of Arkhangai province/, and use questionnaire sheet and HCV Rapid Test for determine risk factor and HCV infection. The study was processed by SPSS-16 program.

The survey has involved among 464 participants aged 40-65 from 7 soum of Arkhangai province. The average ages of participants were 49.6 ± 6.86. 44.6 percent was male participants from total 30.4 percent of participants were 40-44 year old. Participants who have basic education proportion were 34.9 percent and proportion of complete secondary education was 32.8 percent.

20.3 percent of participants were infected with hepatitis C. From total number of participants who had a HCV infection was, infected from unsafe syringe rate was 83.3 percent, participants live with a person who has hepatitis C over the past year infection rate was 50 percent, proportion of participants which infected HCV in non-hospital condition rate was 33.3 percent, participants which infected from HCV infected mother rate was 31.3 percent, the wound was laid stitches infection rate was 25 percent, and proportion of during dental health care services infection rate was above 25 percent. 74.2 percent of participants were not known whether they were infected or not. Risk factor study shows 75 percent of participants were taking health care services in Dental clinic /removed their teeth etc. /, 41.2 percent of participants had been in operation in Hospital, 37.6 percent of respondents had syringe injection in non-hospital condition, 27.3 percent of participants had any dental service, 20.2 percent of participants had a wound sutures.
Dominant risk factors for women were tooth extraction and cosmetic surgery. Dominant risk factors for men are tattoo and changing razors.

14.7 percent of participants haven’t any risk factors, 30.8 percent of respondents have one risk factor, and 0.5 percent of respondents have nine risk factors.

The average respondent of study has 2.3 risk factors. The average infected respondent of study has 2.8 risk factors. The infected person’s risk factor is more than non-infected person’s risk factor. /p=0.019/. The women’s risk factor is 2.51. From total participants who had above 7 risk factors infection rate was 35.7 percent.

The prevalence of anti-HCV was 20.3% among the participant. Average number of people who had a risk factor was 2.3, and infected average person of study was 2.8 risk factors. The most prevalence risk factor is dental service. Prevalence rate is 75 percent.

A phase 2 dose-optimization study of lonafarnib with ritonavir for the treatment of chronic delta hepatitis-end of treatment results drom the LOWR HDV-2 study

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Lonafarnib (LNF) is an oral prenylation inhibitor with demonstrated efficacy in patients infected with hepatitis delta virus (HDV). This class of agents is known to be associated with gastrointestinal side effects. Results of the LOnafarnib With Ritonavir for HDV (LOWR HDV-1) study demonstrated that co-administering LNF with ritonavir (RTV), an inhibitor of LNF metabolism, increases the post-absorption levels of LNF, yielding greater efficacy with lower LNF doses compared to LNF monotherapy. The aim of LOWR HDV2 is to identify optimal combination regimens of LNF and RTV ± PEG-IFNα with efficacy and tolerability for longer term dosing to induce clinically meaningful reductions in HDV-RNA and ALT normalization, or enable HDV-RNA clearance.

48 patients to date have been enrolled in 3 groups of LNF in combination with RTV ± PEG-IFNα for 12 or 24 weeks, followed by 24 weeks of treatment-free follow-up (FU). Groups were divided into high dose LNF (≥75 mg BID) + RTV 100 mg BID (n = 15, 12 weeks), low dose LNF (25 or 50 mg BID) + RTV 100 mg BID (n = 20, 24 weeks) and low dose LNF (25 or 50 mg BID) + RTV 100 mg BID + PEG-IFNα 180 mgg QW (n = 13, 24 weeks). Biochemical parameters and quantitative serum HDV-RNA viral loads were measured.

Low dose regiments hand comparable antiviral efficacy with less GI side effects than the high dose regiments. On 24-week treatment, LNF 25 mg BID +RTV resulted in a mean log decline of -1.74 (±1.20 log10 U/ml), comparable to the historical response to PEG-INFα observed in HIDIT-2. LNF 25 mg BID + RTV + PEG-INFα, however, resulted in a mean log decline of -5.57 (±1.99 log10 U/ml), with 3 of 5 (60%) subjects becoming HDV-RNA PCR-negative and 5 of 5 (100%) of subjects achieving HDV-RNA BLOQ. 2 of 11 (18%)
subjects who completed 12 weeks of LNF 50 mg BID + RTV to date became HDV-RNA PCR-negative. 9 of 15 (60%) subjects with elevated baseline ALT have normalized ALT at Week 24. LNF 25 or 50 mg BID based regiments were associated with mostly grade 1 GI AEs. Results from EOT and FU visits will be presented.

Low dose LNF (25 or 50 mg BID) with RTV ± PEG-INFα including all-oral LNF 50 mg BID + RTV, lead to HDV-RNA PCR-negativity. LNF 25 mg BID + RTV + PEG-INFα leads to the highest rate of HDV-RNA PCR negativity on 24-weeks treatment, and suggests that LNF and PEG-INFα have synergistic activity. These regiments are generally well-tolerated, supporting longer duration studies of greater than 24 weeks, which may lead to HDV cure.

Serum hepatitis B core antibody as a novel tool to assess hepatic inflammation

Our previous studies unexpectedly indicated that the level of serum hepatitis B core antibody (anti-HBc) was positively correlated with the serum alanine aminotransferase (ALT) level. The aim of this study was to determine whether anti-HBc could serve as a potential biomarker for the detection of liver inflammation in chronic hepatitis B (CHB) patients, especially in patients with normal ALT levels.

Serum anti-HBc levels were quantified in 655 treatment-naïve CHB patients, including 45 patients who underwent two liver biopsies (baseline phase and the 78th weeks of antiviral-treatment).

Serum anti-HBc levels were correlated positively with the severity of liver inflammation (r=0.523, P<0.001). After antiviral-treatment, patients with liver inflammation reduction had significant decline in serum antiHBc level. Multivariate analysis showed that anti-HBc was independently associated with moderate-to-severe hepatic inflammation (odds ratio=5.60) in patients with normal ALT level. Furthermore, serum antiHBc showed a high diagnostic accuracy (area under the curve, AUC=0.79) for the differentiation between mild or no inflammation and moderate-to-severe inflammation in patients with normal ALT levels.

Anti-HBc may be a strong indicator for assessing the hepatic inflammatory degree and used for antiviral treatment decisions in CHB patients with normal ALT levels.
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Mongolia has one of the highest rates of viral hepatitis in the world, leading to the highest rate of liver cancer (HCC) in the world. More than 77% of the Mongolian population is estimated to have been infected with hepatitis B virus (HBV) at some time during their life. Tenofovir disoproxil fumarate (TDF) is a potent nucleotide analog recommended as a first line therapy for chronic hepatitis B (CHB) in international guidelines.

The objective of the present study was to assess the effectiveness of the nucleoside analogue TDF in the treatment of chronic HBV.

We followed and evaluated treatment outcome of patients with chronic hepatitis B, initiating their TDF regimen in Happy Veritas Clinic and Diagnostic Center. Only the data of the first 18-months of treatment were considered. A total of 399 patients (218 males and 181 females; age range, 17-81 years; average age, 42 ± 11 years) enrolled in the present study. The assessment of response to treatment after a year was performed using available data relating to viral load (VL) (quantitative HBV-DNA), quantification of HBsAg, Alanine Aminotransferase (ALT) and Transient Elastography (TE). All results are expressed as the median (Q25; Q75). All statistical analyses were performed using the SPSS, version 18.0 software.

According to inclusion and exclusion criteria, a total of 399 patients (218 males and 181 females) enrolled in the present study. The age range of the patients was 17-81 years. The ALT level range of the patients before treatment was 10-392 IU/l, with an average level of 47 (29; 88) IU/l. Among the 399 patients 176 had ALT levels of < 40 IU/l and 223 had an ALT levels of > 41 IU/l. After 18 months the range of ALT level of the patients was from 12 to 160 IU/l, with an average level of 36 (26; 57) IU/l and 231 patients had ALT levels up to 40 IU/l, 168 patients had an ALT levels more than 41 IU/l.

The distribution of patients in different fibrosis stages was: F0 - 40% (n=85), F1 – 9% (n=19), F2 – 23% (n=84), F3 – 18% (n=39), F4 – 21% (n=21). By month 12,71% of the patients with available data (n=175) had HBV-DNA <30 IU/mL, 25% were decreasing and 3% were increased HBV-DNA quantity. Mean HBsAg quantity were increased from 2409 to 3253 IU/mL.

Treatment of HBV using TDF in Mongolia is started only few years ago. We were able to include 12-18-months treatment stage in this study. Our patients were inactive to give their follow up tests. TDF shows significant antiviral activity against HBV. But quantity of HBsAg was increased. And ALT level was increased in 12 months and decreased in 18 months. Therefore, we need to study deep to understand the reason of elevation of ALT and HBsAg quantity. For patients who had fibrosis stage lower than F2 after treatment TE
result decreased. And for patients who had a higher fibrosis stage (up to F3 stage) liver stiffness has increased.

Pathik Parikh, Aabha Nagral, Nishtha Nagral

Patients with Thalassemia major are transfusion dependent and therefore at a high risk of acquiring Hepatitis C infection. The available data on treatment with pegylated interferon as monotherapy or as combined therapy with Ribavirin has shown poor efficacy and tolerability. With the advent of DAA (Directly Acting Antivirals) the picture is likely to change. There is sparse data of treating hepatitis C in thalassemia major with DAA. The present study is carried out to see the safety and efficacy of DAA in this population.

In this prospective study, patients more than 18 years of age with Thalassemia major and a positive Hepatitis C antibody from 5 transfusion centers in Mumbai between January 2016 and August 2016 were studied. In patients with detectable viral RNA by COBAS Taqman PCR, the evaluation included a detailed history including their chelation and blood transfusion requirements. They were investigated with hemogram, liver profile, creatinine, blood sugars, hepatitis C genotype, Fibroscan, ultrasound, MRI liver/heart. They were treated with Sofosbuvir and either of Daclatasvir or Ledipasvir as per genotypes 3 and 1 respectively. Ribavirin was added to genotype 1 as per standard guidelines while it was added to all genotype 3 patients who were treatment experienced, had cirrhosis or had a Fibroscan value >8 kPa. They were followed up till 12 weeks post treatment to determine sustained virological response (SVR12). Clinical and biochemical parameters were observed up until the study period. All statistics were done using SPSS 20 software.

Twenty nine patients were treated during the study period (Mean age 24 years, 16 males, 17 genotype 1, 11 genotype 3, 1 unclassified). During the course of treatment there was significant increase in blood transfusion requirements (28%, 896 vs 1074 ml/month, p=0.0003) in 62% patients and bilirubin levels (p=0.00027) while there was significant fall in hemoglobin, ALT and AST levels (p<0.05). 100% patients achieved SVR. At 12 weeks post treatment as compared to baseline there was significant fall in serum Ferritin levels (p=0.03) while there was no difference in hemoglobin or blood transfusion requirements (p>0.05). There was a trend towards higher chelation requirement throughout the study period but the difference was not significant. Headache, fatigue and diarrhea were the most common side effects (>20% each). None developed serious adverse drug reactions requiring early termination of therapy. The difference in side effects between patients who received Ribavirin (19/29) and those who did not receive Ribavirin (10/29) was not significant.

Direct acting antivirals are safe in thalassemia major patients with Hepatitis C with efficacy of 100% at 12 weeks after stopping treatment. Serum ferritin levels fall significantly after the treatment despite an increase in blood transfusion requirement.
Pharmacokinetics, safety and antiviral activity of CMX157, a novel prodrug of tenofovir, administered as ascending multiple doses to healthy volunteers and


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CMX157 is a novel pro drug of the acyclic nucleotide phosphonate tenofovir (TFV). By converting TFV into a lipid moiety, there is an increase in oral bio availability, targeted cellular uptake through natural lipid absorption pathways and cellular conversion of CMX157 into TFV di-phosphate. A single dose rat study of 20mg/kg CMX157 demonstrated 86% first pass liver extraction. This experiment along with preclinical safety, ADME, and early toxicology results lead to the development of a clinical program. The present, multiple dose, studies were designed to investigate safety, pharmacokinetics and HBV antiviral effects of CMX157.

In the phase 1 study, multiple ascending oral doses of 5, 10, 25, 50, and 100 mg CMX157 were administered sequentially to cohorts of 10 healthy subjects randomized 8:2, active: placebo for 14 days. In the proof of concept study , multiple ascending oral doses of 5, 10, 25, 50, and 100 mg CMX157 were administered sequentially to cohorts of 12 HBV-infected subjects randomized 10:2, CMX157: Viread® for 28 days. Plasma levels of CMX157 and TFV were quantitated using a validated LC-MS/MS assay. Serum levels of HBV DNA were quantitated using the COBAS® AmpliPrep/COBAS®Taqman® HBV Test v2.

Data from day 1 single dose of the 5, 10, 25, 50, and 100 mg CMX157 cohorts in the healthy volunteer study shows CMX157 was rapidly adsorbed and eliminated. T_{max} and t_{1/2} ranged across the cohorts as follows: 2.03.1 hr and 1.1-2.1 hr. Plasma exposure, AUC_{0-∞} and C_{max}, of CMX157 was dose-proportional. AUC_{0-∞} and C_{max} ranges were 10.0-261 hr*ng/mL and 3.1-11- ng/mL across the five cohorts. Data from the day 1 single dose of 5, 10, 25, and 50 mg cohorts in the HBV-infected subject study shows CMX157 was rapidly absorbed and eliminated similar to healthy volunteers. T_{max} and t_{1/2} ranged across the cohorts were as follows: 2.0-2.5 hr and 1.0-1.3 hr. Plasma exposure, AUC_{0-∞} and C_{max}, of CMX157 was dose-related. AUC_{0-∞} and C_{max} ranges were 2.3-112 hr*ng/mL and 2.5-52.2 ng/mL across the four cohorts. CMX157 100 mg HBV-infected cohort data, steady state PK parameters for CMX157 and TFV, safety, and HBV DNA data will also be presented.
CMX157 appeared to be safe and well tolerated on these studies. Consistent with a liver targeted approach, systemic exposure of parent drug and metabolite was low. The favorable safety profiles, PK profiles and in vitro anti-viral results warrant further clinical development of CMX157 in HBV-infected patients.

G. Ulzmaa¹, D. Badamsuren¹, B. Tserendash²

To compare the new method that evaluate prognosis of liver failure with the traditional method.

The 23th October 2016 our study was proved by meeting of biochemical principles (notary in 47) in HSUM. 322 patients with liver cirrhosis who had been in department of gastroenterology of Shastin’s central hospital were evaluated. Before treatment we took the sample of hematology, biochemistry and coagulation. Laboratory examination performed by Sysmex-KX 21, Biochemistry by Humalizer 2000, for the coagulation we used Humaclot apparatus. All statistical analysis were conducted with the SPSS 19.0.

Among all cases 39.34% of patients were in group A, 50.82% in group B, 9.84% in group C according to the Child Pugh classification. For the MELD score 10.93% of patients were in up to 10 score, 73.22% were in 10-19, 13.66% were in 20-29, 2.19% were in 30-39 score and there was no patients who had over 40 score. In the MELD classification total bilirubin or liver functional test indicate jaundice, INR point to coagulation, creatinine shows renal function thus it is more sensitive than the Child Pugh. Therefore we have some idea other researchers. PLT was 119.2±6.25 in A group according to the Child Pugh whereas PLT was 132.31±16.74*10⁹/l in 0-9 score group in the MELD, PLT% was 26.99±1.35 in A group and 26.74±2.29 in 0-9 score of MELD, prothrombin time was 17.37±0.39 in A group and 16.36±0.91 in 0-9 score of MELD. The splenic length was 12.15±0.21 in A group whereas 11.78±0.53 in 0-9 score of MELD. This shows MELD classification enable to make early diagnosis and evaluate the prognosis therefore appropriate other researchers. In 2001 (Kamath et al) according to MELD the death within 3 months happened 27% of patients from lower 20 score and 73% of patients from higher 20 score. In our investigation 13.66% of studied patients requires urgent liver transplantation.
Determination of liver fibrosis stage by fib-4 in patients with chronic viral hepatitis

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³ I

Objectives:
There from in last year’s hepatocellular carcinoma is most common malignancy, first of all cancers in Mongolia. Liver fibrosis leading to portal hypertension, and it can increase risk of hepatocellular carcinoma. Liver fibrosis is the accumulation of extracellular matrix in response to acute or chronic liver injury. Measurement of fibrosis helps to stage the severity of disease, it allows serial determination of disease progression and may play an important role in clinical management and determine patients prognosis. The aim of this study is to determine liver fibrosis stage by non-invasive serum biomarker FIB-4 in patients with chronic viral hepatitis.

Methods:
130 cases by chronic viral hepatitis at third central hospital in Mongolia from retrospectively reviewed and analysed. The clinical data including AST, ALT and platelet count were recorded. FIB-4 was calculated.

Result:
From all, males 47% and females 53%, with mean age of 49.72±14.3. All of the causes are HCV 63.85%, HBV 32.31%, HCV+HBV co-infection 3.85%. In cases of mean value of platelet count, ALT, AST was 211.18±72.9, 112.5±162.4, 82.37±101.5, respectively. FIB-4 was detected <1.45 cutoff value 48.46% non-fibrosis (F0 to F1 by Metavir), 1.45-3.25 score 33.08% fibrosis (F2 to F3 by Metavir), >3.25 cutoff value (F4 by Metavir) 18.46% cirrhosis. 31 (37.34%), 11 (26.19%), 3 (20%) cases of fibrosis were determined in patients with HCV, HBV, HCV+HBV co-infection, respectively.

Conclusion:
1. Recorded data ALT, AST of chronic viral hepatitis were detected 112.5±162.4, 82.37±101.5 respectively.
2. In patients with chronic viral hepatitis, HCV FIB-4 was determined fibrosis in 43, 31 cases, respectively.

Validation of the PAGE-B model in Asian chronic hepatitis B patients receiving entecavir or tenofovir

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A new hepatocellular carcinoma (HCC) risk prediction model, PAGE-B, which includes age, gender, and platelet count as constituent variables, has recently been proposed in Caucasian chronic hepatitis B (CHB) patients. We validated the PAGE-B model and compared its accuracy with that of conventional risk prediction models in Asian CHB patients.
Methods:

A new hepatocellular carcinoma (HCC) risk prediction model, PAGE-B, which includes age, gender, and platelet count as constituent variables, has recently been proposed in Caucasian chronic hepatitis B (CHB) patients. We validated the PAGE-B model and compared its accuracy with that of conventional risk prediction models in Asian CHB patients.

Results:

A total of 1092 CHB patients (668 men, 61.2%) were selected between August 2006 and January 2015. The mean age was 48 years. During the follow-up period (median, 43.6 months), 36 (3.3%) patients developed HCC. Older age (hazard ratio (HR) = 1069), male gender (HR = 3.054), cirrhosis (HR = 4.306), and a lower platelet count (HR = 0.991) were independent predictors of HCC development. PAGE-B showed similar area under receiver operating characteristic curves (AUROCs) to GAG-HCC and CU-HCC at 3 years (0.777 vs. 0.793 and 0.743, respectively; all P>0.05) and 5 years (0.799 vs. 0.803 and 0.744, respectively; all P>0.05), whereas the AUROCs of PAGE-B were significantly higher than those of REACH-B (0.602 at 3 years and 0.572 at 5 years, P<0.05). When cirrhosis was incorporated into PAGE-B (modified PAGE-B), its predictive performance became significantly higher than that of PAGE-B at 5 years (P<0.05).

Conclusions:

Our study demonstrated that PAGE-B is applicable to Asian CHB patients and has similar accuracy to conventional risk prediction models. Further studies are warranted to establish strategies for HCC surveillance using PAGE-B in CHB patients.

Maralmaa Enkhbat¹², Ganbolor Jargalsaikhan¹², Bekhbold Dashtseren¹², Batdelger Dendev¹², Purevjargal Bat-Ulzii¹², Delgerbat Boldbaatar¹², Zulkhuu Genden¹², Surenkhuu Narankhuu¹², Ayush Dagvadorj¹, Dahgwanhdorj Yagaanbuyant¹², Andreas Bungert², Naranjargal Dashdorj¹, Naranbaatar Dashdorj²

Background and objective:

Mongolia has one of the highest rates of liver cancer mortality worldwide. The high prevalence of chronic hepatitis C is one of the main causes for Mongolia’s world leading liver cancer mortality rate. Direct Acting Antivirals for treatment of HCV have become available in Mongolia in 2015. Since then, a large number of HCV infected patients with or without advanced liver disease has been successfully treated with the combination of Ledipasvir/Sofosbuvir. The aim of this study is assess the rate of sustained viral response (SVR) in patients with advanced cirrhosis.

We included patients diagnosed with HCV infection and cirrhosis, who enrolled into treatment with Sofosbuvir/Ledipasvir regimen at the Liver Center, Ulaanbaatar, Mongolia between December of 2015 and September of 2016. Cirrhosis was determined using Fibroscan (cirrhosis: ≥14.6 kPa). SVR was assessed at 12 weeks after the end of the treatment. A total of 42 patients with cirrhosis including, 27 (64.2%) female, mean age 55.1±9.9 (36 to 76), was included in the study. Before treatment results of HCV-RNA count, haematology biochemistry, abdominal ultrasound, AFP, Fibroscan and urine analysis, respectively, were collected. All patients received a combination therapy of SOF/LED for 24 weeks.
4 of 42 patients had previously treated with peg-interferon, 35 (83%) patients was CTP-A, 5 (11.9%) - CTP-B and 2 (4.7%) was CTP-C, all patients had HCV genotype 1b. Overall, 40 (95%) patients achieved SVR, 2 (4.8%) patients, are failed to achieve SVR. One of these patient is CTP-C and MELD score- 13 and other was CTP-A. In 40 of 42 patients ALT/AST reached the normal level. Fibroscan values were decreased in in 20 patients by an average of 45% at the end of the treatment.

The DAAs (SOF/LED) are impressively effective indicated by a SVR rate of 95% in patients with cirrhosis.

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**Conclusion:** The DAAs (SOF/LED) are impressively effective indicated by a SVR rate of 95% in patients with cirrhosis.

Clinical outcomes were comparable between chronic hepatitis B patients with virological response using oral antiviral therapy and inactive carriers when adjusting for fibrotic burden


**Background and objective:** We aimed to compare the risk of developing hepatocellular carcinoma (HCC) between patients with chronic hepatits B (CHB) who achieved virological response (VR) by nucleos(t)ide analogues (NUC) (NUCVR group) and patients with inactive CB phase (ICHBP group), after adjusting for fibrotic burden by liver stiffness (LS) using transient elastography (TE).

**Methods:** To adjust for imbalance between NUC-Vr group (n=1291) and ICHBP group (n=741), propensity-score matching (PSM) was performed at 1:1 ratio, based upon following variables: age, gender, diabetes, platelet count, albumin, total bilirubin, ultrasonographic cirrhosis and LS at VR. VR was defined as serum HBV-DNA <2.000 IU/mL with biochemical response (normal serum ALT level). After PSM was performed, cumulative rates of HCC development were assessed using Kaplan-Meier analysis with a comparison by the method of Klein and Moeschberger.

**Results:** Among entire population, ICHBP group had a lower risk pf HCC development (p<0.001 by log-rank test). However, when we stratified entire population according to the presence of cirrhosis, owing to the significantly higher incidence of HCC in cirrhosis patients, cumulative rates of HCC development in cirrhotic patients (n=6 28) were similar between NUC-VR group and ICHBP group and similar results were obtained for non-cirrhotic patients (n=1404) (both p>0.05 by log-rank test). PSM was performed, resulting in 610 pairs and cumulative rates of HCC development were similar between NUC-VR group and ICHBP group (p>0.05).

**Conclusions:** Clinical outcomes were comparable between CHB patients with VR using NUCs therapy and inactive CHB carriers when adjusting for fibrotic burden. Our results strongly support the clinical importance of appropriate HBV suppression using antiviral therapy.

Quantitative HBsAg level in HDV infected Mongolian patients

**Sarantuya Gidaagaya**, **Uranbaigal Enkhbayar**, **Ariunaa Bayarjargal**, **Sumiya Dorj**, **Munkhbat Batmunkh**, **Bira Namdag**
Background: The study from 10 years ago has shown that the prevalence of HBV infection in Mongolia was 9.6 and one third of HBsAg carriers were co-infected with HDV. Quantification of serum HBsAg has several clinical significances such as acting as a biomarker for the hepatitis D virus (HDV)-RNA level and necroinflammatory activity in HDV infection.

Objectives: The aim of this study was to determine seroprevalence of HDV infection among HBsAg positive Mongolian patients and compare quantitative HBsAg levels in HBV mono-infected and HBV/HDV dual infected individuals.

Methods: Serum samples were collected from 373 HBsAg positive individuals for two year period. Serum samples were screened for IgG antibodies to hepatitis delta virus (HDV) using enzyme-linked immunosorbent assay (ELISA) method. Serum HBsAg level was measured using commercial tests.

Results: Anti-HDV IgG and IgM antibodies were detected in 315 (84.5%) and 183 (49.1%) individuals aged from 22-70 years. We compared demographic and laboratory characteristics in HBV mono-infected (n=58) and HBV/HDV dual infected patients (n=315). Median age of HBV mono-infected group was 38 whereas 40 in HBV/HDV dual infected group (p=0.007). Sex and HBeAg distribution was similar in both groups. The mean WBC and PLT levels were significantly lower in HBV/HDV dual patients than the HBV infected (5.1 ±1.5 x 10^6/L vs. 6.2 ±1.8 x 10^6/L, p < 0.001; 189 ±67 x 10^9/L vs. 228 ±70 x 10^9/L, p <0.001). Higher transaminase level was observed more in dual infected patients than HBV mono-infection. Dual infected group has higher number of cirrhotic patients than HBV mono infected group (45.6% vs. 12.1%, p < 0.001). The number of patients with qHBsAg >2000 IU/mL was significantly higher in the HBV/HDV dual infected group (76.8%) than the HBV mono-infected group (63.8%, p = 0.029). Mean HBsAg levels in HBeAg positive subjects were comparable between two groups (4.3 ±0.4 log IU/mL vs. 3.2 ±1.0 log IU/mL, p = 0.1). On the other hand, qHBsAg levels in HBeAg negative dual infected patients were 3.5 ±0.8 log IU/mL and were 3.2 ±1.0 log IU/mL in HBeAg negative HBV mono-infected subjects (p=0.013).

Conclusion: We concluded that the HDV infection rate in Mongolia is extremely high and further investigation is needed to validate the finding. High level (>2000IU/mL) of quantitative HBsAg level was observed frequently in HBV/HDV dual infected groups.
The viral hepatitis is endemic in Mongolia. The morbidity and mortality of HBV is decreased in the last 10 years in the result of vaccination against viral hepatitis B, which is used since 1991. Every year, in Mongolia less than 100 new cases of HDV infection is registrates. The aim of the study was to analyze the current situation of HDV infection, which was occurring in Mongolia during 2014-2016 years.

**Methods:**
The descriptive study was done 217 histories of patients, who were treating in National Center for Communicable diseases with diagnosis “co” and “super” Delta hepatitis during 2014-2016 years. The SPSS21 program was used for the data analysis.

**Results:**
The 1.8% (n=4) of all cases (n=217) has co-infection of HDV, 98.2% (n=213) - super-infection. The average age of patients was 28±6.9 years and 70.2% was male, 29.8% - female. The occurrence of HDV infection dominated in 20-34 years old (78.8%), 3.7% - 0-19 years, 15.9%-35-54 years old. The contact and transmission way were uncertain in 85.3% of cases. 14.7% of all cases had an epidemiological anamnesis such as medical surgery (60.6%), dental treatment (24.4%), cosmetic surgery (6%), family contact (9%) and 1 case was diagnosed during the observation of pregnancy. The HBV/HDV co-infection was confirmed by detecting HBsAg, HBeAg, anti-HBc-IgM, anti-HBc, anti-HBe, anti-HDV-IgM and anti-HDV. In all patients were not checked the HDV-RNA and were not used antiviral treatment.

**Conclusion:**
The super-HDV infection is dominating among the young male between 20-34 years old. In most cases (82.5%) contact and transmission way of infection is uncertain. There is necessity to improve diagnostic and treatment capacity of NCCD for the HDV infection.

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**Active versus passive follow-up examination of patients with chronic hepatitis C during Sofosbuvir/Ledipasvir treatment**


**Objectives:**

The super-HDV infection is dominating among the young male between 20-34 years old. In most cases (82.5%) contact and transmission way of infection is uncertain. There is necessity to improve diagnostic and treatment capacity of NCCD for the HDV infection.
In Mongolia, Sofosbuvir/Ledipasvir (SOF/LED) was officially approved for the treatment of people with chronic HCV infection in April of 2015 and branded and generic versions were made available in January and May of 2016, respectively. As of September 2016, 4681 patients had received SOF/LED treatment. However, some these patients did not undergo regular follow-up examinations during the treatment because of cost and other concerns. In this study, we aim to assess differences in sustained viral response (SVR) between the active and passive follow-up groups.

Methods: We selected a total of non-cirrhotic 80 patients (aged 54.7±12.03, 51 female, 29 male) who received SOF/LED combination. Inclusion criteria of this study were an APRI score of less than 2.0 or a FIB-4 score of less than 3.25. This group of 80 patients was divided into 2 groups, namely active and passive follow-up. In the active follow-up group, we determined clinical and biochemical parameters and HCV-RNA prior to the start of the treatment, at the 4th week and the 12th week of treatment. In the passive follow-up group, we determined clinical and biochemical parameters and HCV-RNA only at the beginning of the treatment. In both the active and passive follow-up groups, we determined SVR for all patients 12 weeks after the end of the treatment (EOT).

Results: All patients (100%) achieved SVR at 12 weeks after the EOT. Virological and functional outcomes of the patients are shown in Table 1. AST and ALT levels, and APRI and FIB-4 scores decreased significantly during treatment (p<0.001) in the active follow-up group.

Conclusions: Antiviral treatment with SOF/LED enabled elimination of HCV in patients without cirrhosis. Successful treatment was associated with significant improvement of the enzymatic liver function. There was no difference of SVR rate between the active versus passive follow-up groups. Relinquishing active follow-up during treatment may be an option for patients without cirrhosis. This can increase access to HCV cure in a country like Mongolia, where costs for diagnostics are at a similar level as treatment.

Table 1. Laboratory results of 2 groups during the SOF/LED treatment

<table>
<thead>
<tr>
<th></th>
<th>Active follow-up group (40 patients)</th>
<th>Passive follow-up group (40 patients)</th>
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<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>th 4 week</td>
</tr>
<tr>
<td>Mean age</td>
<td>54.7±12.03 (32-76 years)</td>
<td>52.2±12.6 (23-81 years)</td>
</tr>
<tr>
<td>APRI score</td>
<td>0.8±0.5 (0.2-2.4)</td>
<td>0.4±0.3 (0.1-1.9)</td>
</tr>
<tr>
<td>FIB-4</td>
<td>1.9±1.3 (0.5-8.1)</td>
<td>1.4±0.9 (0.4-5.0)</td>
</tr>
<tr>
<td>HCV-RNA</td>
<td>1.9<em>6log±2.3</em>6log IU/mL (2<em>2log-1.1</em>7log)</td>
<td>10.1±14.7 IU/mL (0-86)</td>
</tr>
<tr>
<td>AST</td>
<td>65.9±42.0 u/L (13-201.6)</td>
<td>30.7±24.4 u/L (10.7-134.2)</td>
</tr>
<tr>
<td>ALT</td>
<td>104.9±81.9 u/L (13.1-351)</td>
<td>39.6±42.5 u/L (8.1-225)</td>
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</table>
### Total Bilirubin
<table>
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<tr>
<th></th>
<th>17.6±12.4 umol/L (5.8-76.6)</th>
<th>15.6±8.3 umol/L (3-43.9)</th>
<th>14.9±6.3 umol/L (1.0-29.7)</th>
<th>14.9±5.4 umol/L (5.8-29.5)</th>
</tr>
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</table>

### PLT (10 /L)
|               | 204.2±47.4 (128-326)       | 204.6±44.1 (128-293)     | 220±44.9 (130-365)         | 217.9±45.1 (108-304)       |

### SVR rate
|               | 40/40 (100%)               | 40/40 (100%)             |                             |                             |

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**A nationwide seroprevalence of hepatitis A in Republic of Korea from 2005 to 2014, before and after peak outbreak in 2009**

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The epidemiologic shift of hepatitis A virus (HAV) infection in the South Korean population resulted in the peak outbreak of hepatitis in 2009. The aim of this study was to clarify the seroprevalence of anti-HAV antibody (anti-HAV) and its demographic characteristics before and after the peak outbreak from 2005 to 2014.

This retrospective study analyzed the nationwide anti-HAV data of all the requested cases from 1,795 medical institutions to a major central laboratory (Seoul Clinical Laboratories) during January 2005 and December 2014. The prevalence of anti-HAV was adjusted for age and area with the standard population based on the 2010 Census data from Korea National Statistical Office.

A total of 424,245 cases were included in this study. The overall age-adjusted anti-HAV prevalence decreased from 65.6% in 2005 to 62.2% in 2014. During the 10 years, the age-specific seroprevalence continuously decreased in persons aged 30 to 39 years (69.6% to 32.4%) and those aged 40-49 year (97.9% to 79.3%). In contrast, it increased in persons aged 10 to 19 years (15.4% to 35.2%), while it reached a trough (8.7%) in 2010 and rebounded to 20.2% in 2014 persons aged 20 to 29 years.

The overall age and area-adjusted seroprevalence of anti-HAV decreased from 65.6% to 62.2% from 2005 to 2014 in South Korea. Persons aged 20-39 years are currently most vulnerable to HAV infection, and more severe clinical manifestations of hepatitis A is expected in more aged population (30-49 years). The dynamic change of HAV epidemiology should be monitored to establish optimal presentive measures.
Seroprevalence and clinical characteristics of viral hepatitis in transfusion-dependent thalassemia and hemophilia patients

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Transfusion dependent subjects are at a great risk of viral hepatitis infection. We aimed to evaluate the prevalence and factors associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) infection among transfusion-dependent patients in Taiwan.

A total of 140 patients (67 thalassemic patients, 70 hemophilic patients, two patients with hereditary spherocytosis and one patient with von Willebrand disease) were prospectively enrolled to evaluate the prevalence and factors associated with viral hepatitis and spontaneous HCV clearance. All patients were tested for HBV and HCV serology and virology. Two consecutive serum samples, at least 1 year apart, were collected to clarify HCV seroclearance.

The seropositivity rate of hepatitis B surface antigen (HBsAg), HCV antibody (anti-HCV), and both HBsAg/anti-HCV were 6.4%, 45.7% and 5%, respectively. Logistic regression analysis of factors associated with anti-HCV seropositivity included age (odds ratio/95% confidence interval [OR/CI]: 1.11/1.06-1.17, P<0.001), serum alanine aminotransferase (ALT) (OR/CI: 1.05/1.03-1.08, P<0.001) and platelet counts (OR/CI: 0.995/0.991-0.998, P=0.002). Age was the only factor independently associated with HBsAg seropositivity (OR/CI: 1.08/1.02-1.14, P=0.007). Compared to patients born before 1992, the seroprevalence of HCV among thalassemic patients decreased dramatically in those born after 1992 (46.0% vs. 11.8%, P=0.012). The seroprevalence of HCV among hemophilic patients also decreased significantly when comparing patients born before 1987 to those born after 1987 (79.5% vs. 11.5%, P<0.001). Similarly, the seroprevalence of HBV decreased significantly in the post-vaccination cohort compared to its counterpart (13.1% vs. 1.3%, P=0.005). The spontaneous clearance of HCV was observed in 25.4% (15/59) of patients, and ALT was the only factor associated with it (OR/CI 0.98/0.96-1.00, P=0.02).

Both HBV and HCV infections are prevalent among transfusion-dependent thalassemic and hemophilic patients in Taiwan. Nevertheless, seroprevalence decreased significantly and dramatically for HCV after universal blood screening and for HBV after implementation of a universal mass vaccination program.
Role of Fibroscan and APRI score in detection of liver fibrosis in patients with hepatitis B in Ulaanbaatar

Gerelchimeg Tsagaantsooj¹,², Baatarkhuu Oidov², and Amarsanaa Jazag¹

¹Happy Veritas Clinic and Diagnostic Center ²Mongolian National University of Medical Sciences

The assessment of liver fibrosis is essential for predicting the prognosis and outcome of all forms of chronic liver disease. A liver biopsy is the gold standard for the assessment of liver fibrosis, but it has its limitations, which include life-threatening complications. Alternative methods of non-invasive laboratory and radiological testing for the assessment of liver fibrosis in hepatitis have evolved during the past decade, and these methods may be able to overcome the limitations of liver biopsy.

This study was conducted in order to assess liver fibrosis using Fibroscan, and to compare these results to the AST platelet ratio index (APRI scores) on HBV patients.

A cross-sectional study was conducted on HBV patients who underwent Fibroscan examinations between March 15, 2015 and February 30, 2017 in Happy Veritas Clinic and Diagnostic Center. Demographic data was collected, including sex, age, and nationality; serum alanine aminotransferase levels (ALT, 6 - 24 U/L), serum aspartate aminotransferase levels (AST, 13 - 33 U/L), and platelet counts (180 – 320*10⁹) were also determined. The stages of fibrosis (F0 0 – 7.2, F1 7.2 – 8.2, F2 8.2 – 11, F3 11 - 18.3, and F4 ≥ 18.3) were in kPa. The result of APRI was compared with the Fibroscan fibrosis scores.

The results of 228 patients were analyzed, including 126 (55%) males with a mean age of 42 years (SD: 9.9; range: 22 - 67). The males were significantly younger than the females (47 years (SD: 10.5; range 18 - 72) (P < 0.001)). The mean stiffness score was 11.29 (SD: 8.7) kPa and most patients exhibited no fibrosis (37%) and mild-moderate level (38%) of fibrosis. Thirty patients (13%) had advanced fibrosis. The mean platelet and serum ALT levels were 1.11 (SD: 1.42; range 0.12 - 13.7). There was a significant positive correlation between the Fibroscan results and the APRI scores (P < 0.001). Similarly, there was a significant positive correlation between age and fibrosis score, and a significant negative correlation between platelet count and stiffness score.

This study has shown that the combination of Fibroscan and APRI methods provides a valuable approach for assessing liver fibrosis in patients with hepatitis. This can eliminate the need for liver biopsy in patients without clear indication.
Acute hepatitis C virus infection among HIV-infected men who have sex with men

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Background: It is known that approximately 1 million people are infected with hepatitis C virus (HCV) in Japan. The total number of acute hepatitis C virus infection cases (AHCVI) has decreased, but that of sexually transmitted cases (especially among men who have sex with men: MSM) has increased. In this study, we aim to analyze the molecular basis of HCV transmission among HIV-infected MSM (HIVMSM) by identifying the routes of infection and clarifying of the virological features. Our results could be helpful to prevent HCV transmission by raising awareness among physicians and the public.

Methods: Occurrences of AHCVI were observed among HIVMSM in a clinic at Shinjuku-ku, Tokyo. We compared the sequences of HCV hypervariable region 1 (HVR1) in the sera of AHCVI cases among HIVMSM in the clinic from 2012 to 2016. In addition, the core region of the HCV genome was also amplified by using genotype specific primers to identify the genotype of HCV in HIVMSM.

Results: From 2012 to 2016, the sera of 12 AHCVI cases among HIVMSM were collected and tested for HCV RNA. To characterize the viral populations in the HIVMSM, we analyzed the nucleotide sequence of the amplified HCV cDNA at the N-terminus of the E2 region containing HVR1. HCV genomes from patient 2012A and 2012B in 2012 showed a high homology of 96%. Interestingly, both clones had an identical 3-nucleotide deletion at the junction between the E1 and E2 regions. HCV from patient 2014F and 2014G in 2014 also showed a high homology of 98%. Furthermore, we found highly conserved sequences among HCV clones from patient 2012C in 2012, 2014D, 2014E in 2014, and among patient 2014F, 2014G in 2014, 2016H in 2016. In 6 cases of AHCVI of HIVMSM in 2012 and 2016, co-infection with HCV genotypes 1b and 2a was found.

Conclusions: Awareness of AHCVI reports was raised to HIVMSM patients in public health centers and AIDS clinical hospitals in 2012 and 2014, but occurrences of AHCVI have been still observed since then. It is considered that continued education and prevention efforts are necessary to prevent HCV infection among HIVMSM.

Interrelationship between TFE3 and Rag GTPase C/D depending on nutritional status

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Transcription factor E3 (TFE3) has been shown to increase insulin sensitivity in liver by activating insulin signaling pathways with amelioration of hyperglycemia in mouse models of diabetes. TFE3 is a basic helix-
loop-helix protein that belongs to the microphthalmia associated transcription factor (MiTF) and TFE (MiTF/TFE) family, which include TFEB, MITF, TFEC and TFE3. TFEB and TFE3 are shown to be phosphorylated by mTORC1 by generating a binding site for 14-3-3, a cytosolic chaperone that keeps those transcription factors sequestered in the cytosol. Recently it was reported that MiTF/TFE family might function as critical factors in nutrient sensing and maintenance of cellular homeostasis. In amino acid sufficient state, active Rag GTPase binds the mTORC1 component raptor and recruits mTORC1 to lysosome. In addition, active Rag GTPase interacts with TFE3 and this interaction facilitates the mTORC1-dependent phosphorylation on TFE3. In starvation state, TFE3 is translocated to the nucleus and bound to the CLEAR elements present in the promoter region of varieties of lysosomal genes.

Hypothesis:

Nutrient-sensing pathways are commonly dysregulated in human metabolic disease. It was shown that Rag GTPases are key modulators of amino acid signaling on mTORC1 activity. Since TFE3 interacts with active Rag GTPases and exhibited mTORC1-dependent phosphorylation in repletion state, we hypothesized that transcription factor TFE3 could regulate the gene expression of Rag GTPases.

Methods:

To investigate the target gene of TFE3, micro assay was performed using Affymatrix chip with mouse liver exogenously overexpressing TFE3. ChIP assay and luciferase assay showed that TFE3 activates the RagC/D promoter activity. TFE3 mediated up-regulation of RagC/D was tested using RT-qPCR and western blot assay.

In silico search suggested that there are several CLEAR elements in the Rag GTPase C and D (RagC/D) promoter. In this study, we demonstrate that TFE3 is responsible for the up-regulation of RagC/D gene expression in mouse liver. ChIP assay showed that TFE3 binds directly to RagC/D gene promoter. Transduction of adeno-TFE3 to mouse liver increased RagC/D mRNA and protein level. Interestingly, Adenovirus mediated shTFE3 treatment down-regulated the gene expression of RagC/D Hepa1-6 cell.

From this study, it is concluded that TFE3 activates the gene expression of Rag GTPase C/D by direct binding on the CLEAR element of the promoter. Thus, TFE3 might act as direct transcription factor modulating RagC/D gene expression. Furthermore, it is expected that both TFE3 and Rag GTPase C/D molecules affect to each other through regulating the gene expression and cellular localization, respectively.

Study to determine M2BPGiin serum

G.Enkhmaa¹, Yo.Bumdari²

World Health Organization has estimated more than 5% people infected with chronic HBV and HCV worldwide. The high rate of viral hepatitis transmission worldwide has resulted in an increased incidence of liver cirrhosis, due to diagnosis delay, improper treatment and liver fibrosis associated with persistent HBC and HCV infections irreversibly progressing to chronic hepatitis patients. Although liver fibrosis reflects disease severity in chronic hepatitis patients, there is no simple and accurate methodology on evaluation of treatment efficacy for liver fibrosis. In order to fulfill this requirement, a glycan-based
immunoassay as FastLec-Hepa has been introduced. FastLec-Hera method reveals unique fibrosis-related glyco-alteration hyperglycosylated Mac-2 binding protein in serum.

To determine M2BPGi in serum

A total of 117 patients were randomly involved. Out of all patients, for 34 patients with suspected anamnesis of viral hepatitis were done Blood count testing, liver function testing, HBV, HCV, AFP, HbA1c, and glucose testing. We used HISCL 5000 analyzer, Sysmex, Japan for detection.

We determined of M2BPGi in serum of 117 patients and protein average level was 1.7 ± 2.7 COI (0.10-17.61). A 62 patients were normal, M2BPGi was 0.59 ± 0.20 C.O.I (0.1-0.97), 39 patients were 1+, M2BPGi was 1.51 ± 0.54 C.O.I (1.02-2.91), 16 patients were 2+, M2BPGi was 7.1 ± 4.59 C.O.I (3.03-4.59), respectively.

We determined M2BPGi in patients with HBV and HCV; normal 7 (20.6%), M2BPGi was 0.79 ± 0.17 C.O.I, (0.48-1.0), 1+ 17 (50%), M2BPGi was 1.5 ± 0.49 C.O.I (1.03-2.81), 2+ 10 (29.4%), M2BPGi was 5.3 ± 3.3 C.O.I (3.0-12.3), respectively.

About of half (47%) patients out of all patients involved in the study were with increased M2BPGi level. Majority (79%) of all patients with B and C viral hepatitis were with elevated level of M2BPGi. Detection of M2BPGi will be essential in the prediction of early diagnosis of hepato-cellular carcinoma.

Clinical significance of urinary neutrophil gelatinase-associated lipocalin measurement in differentiating various etiologies of acute kidney injury in cirrhotic patients


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Diagnosis of hepatorenal syndrome (HRC) is frequently delayed while excluding other etiologies of acute kidney injury (AKI). Inappropriate diagnosis of AKI in turn may aggravate the prognosis of a patient. There has been several reports that urinary neutrophil gelatinase-associated lipocalin (u-NGAL) might have a role in differentiating various etiologies of AKI in liver cirrhosis patients. We aimed to assess the clinical significance of u-NGAL measurement in management of AKI that occurs in cirrhotic patients.

Cirrhotic patients who developed AKI were prospectively enrolled between 2015 and 2016. AKI was defined by the definition of International Club of Ascites-Acute Kidney Injury (ICA-AKI). On clinical judgement, AKI was subgrouped into 4 groups according to the etiologies. They were pre-renal type (group 1), HRS (group 2), infection (group 3), and acute tubular necrosis (ATN) (group 4), respectively.

A total of 53 AKI patients were included in this study. Number of patients in each groups were 20, 11, 12 and 10 patients in pre-renal type, HRS, infection and ATN, respectively. The proportion of male was not different among the groups, ranging from 67% to 80%. Number of patients with decompensated cirrhosis (ChildTurcotte-Pugh score ≥7) were 15 (75.0%), 10 (91.0%), 10 (83.4%), and 10 (100%), respectively.
Median serum creatinine (sCr) levels were 1.44 (range, 0.90-2.57) mg/dL, 2.24 (range, 1.24-3.42) mg/dL, 1.79 (range, 1.18-13.17) mg/dL, and 2.69 (range, 1.18-5.65) mg/dL in each of 4 groups. Differences in sCr levels were only significant in comparison between pre-renal type vs. HRS (p<0.001), and prerenal type vs. ATN (p<0.001). However, sCr levels were not different between the HRS and ATN group. Meanwhile, median U-NGAL levels were 29 (range, 10-132), 68 (range, 23-1419), 1061 (range, 241-3000), and 2416 (range, 406-3000) in each of 4 groups. U-NGAL levels showed difference in comparison of any of the two groups among various etiologies except infection vs. ATN. Especially median U-NGAL level of HRS was clearly different from those levels of pre-renal type (p<0.001), infection (p=0.002), and ATN (p<0.001).

Conclusions: Median U-NGAL levels in each groups showed great difference according to etiologies of AKI. Therefore, U-NGAL levels may be helpful in differentiation of HRS from ATN. Cut-off levels of each settings should be defined in a further study with a larger cohort to utilize U-NGAL level in real-life practice.

The prenylation inhibitor lonafarnib can induce post-treatment viral clearance in chronic delta hepatitis resulting in ALT normalization and regression of fibrosis

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Chronic delta hepatitis (CDH) is the most severe form of viral hepatitis, with no adequate therapy. The prenylation inhibitor LNF is the first investigational agent targeted for hepatitis D virus (HDV). Here we report the post-treatment clearance and subsequent follow up course in patients (pts) who were HDV-RNA positive following treatment with 12-24 weeks (wks) of LNF.

27 pts were analyzed who had detectable end of treatment HDV-RNA after receiving LNF for 12-24 wks in the LOWR HDV-1 and LOWR HDV-2 (LONafarnib with Ritonavir for HDV-1 and 2) trials, and who were at least 24 wks post-treatment. A post-treatment ALT flare was defined as elevation of ALT to >2x baseline (BL) level.

Pts came from multiple LNE treatment cohorts: LNF 200 mg bid, 12 wks: LNF 300 mg bid, 12 wks: LNF 100 mg bid + RTV 50 mg bid, 12 wks: LNF 75 mg + RTV 100 mg bid, 12 wks, followed by addition of pegylated interferon alfa, 12 wks: LNF 50 mg bid + RTV 100 mg bid, 24 wks. Following treatment. 5 of 27 (18.5%) pts experienced post-treatment ALT flares (median ALT 190 U/mL, range 110-1355 U/mL), resulting in ALT normalization and HDV-RNA negativity within 12-24 wks. In all 5 pts, HDV-RNA had declined rapidly during LNF treatment, followed by gradual rises on-therapy to near BL levels, associated with decreased LNF exposure (due to dose reductions or excessive GI side effect). HBV DNA levels increased in all 5 pts by at least 3 logs (none had received concomitant nucleotide analog treatment). Post-flare HBV DNA levels were suppressed in all 5 pts (<1000 IU/mL) and undetectable in 2 pts, HBsAg in one patient decreased from 3900 IU/mL to <10 IU/mL Two pts with intermittent low level HDV-RNA (BLOQ) post-ALT flare were retreated.
with 24 wks low dose LNF (LNF50 mg BID+RTV). HDV-RNA PCR-negativity was achieved soon after restarting treatment, and has remained so to date 12 wks post ending retreatment. Fibrosis grade decreased compared to BL from 4 to 3, 2 to 0 and 6 to 4, respectively, in the 3 pts rebiopsied 6-18 months following initial ALT normalization and HDV-RNA negativity.

LNF can induce therapeutic post-treatment immunological flares—a phenomenon heretofore not described in CDH and thereby dramatically alter the natural history of untreated CDH. Thus, at least two pathways for achieving HDV negativity with LNF therapy exist: LNF-induced progressive suppression to HDV negativity on-treatment, and LNF-induced post-treatment anti-HDV therapeutic flares (described here).

Conclusions:

LNF can induce therapeutic post-treatment immunological flares—a phenomenon heretofore not described in CDH and thereby dramatically alter the natural history of untreated CDH. Thus, at least two pathways for achieving HDV negativity with LNF therapy exist: LNF-induced progressive suppression to HDV negativity on-treatment, and LNF-induced post-treatment anti-HDV therapeutic flares (described here).

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**Evaluation of the rapid diagnostic tests to detect anti-HCV**

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**Objectives:** Rapid diagnostic tests (RDTs) to detect HBsAg and anti-HCV could be ideal tools for decentralized HBV and HCV general population hepatitis screening. For example: Within the Screening Campaign of the Hepatitis Prevention, Control, and Elimination Program “Элэг бүтэн Монгол” хөтөлбөр that announced by the Government of Mongolia in April of 2017. In this study, we aimed to evaluate the sensitivity and specificity of the RDTs to detect anti-HCV that are widely used in Mongolia.

**Methods:** The study design was cross-sectional. Total of 270 serum samples which were divided into 3 groups: HBVDNA positive 90 samples, HCV-RNA positive 90 samples, donor 90 samples were assessed by 10 different rapid tests to detect anti-HCV (OraQuick HCV (OraSure, USA), Hexagon (HUMAN, Germany), Cypress (Cypress Diagnostic, Belgium), SD-Bioline (Standart Diagnostics, Korea), Genedia (Green Cross, Korea), Abon (Abon Biopharm, China), Humasis (Humasis, Korea), CTK (CTK Biotech, USA), Wondfo (Wondfo Biotech, China), and InTec (InTec Products, China)). Reference methods were ELISA (DIA.PRO, Italy), and quantative PCR (Abbott m2000rt/sp, USA).

**Results:** The comparative results of the RDTs are shown in Table 1. The OraSure test that is approved by FDA has high sensitivity and specificity. But it is difficult to use because of high price. The following RDTs: Hexagon, Cypress, SD-Bioline, Genedia have 1.1–3.3% false negative results and Abon has high false positive (14.8%) results. Therefore, these RTDs should not be used for the general population screening.

**Conclusions:** The OraQuick has highest sensitivity and specificity for detecting anti-HCV, but Humasis, CTK, Wondfo, InTec RDTs have relatively high sensitivity and specificity with affordable price. So we recommended to use Humasis, CTK, Wondfo, InTec RDTs.
Acoustic radiation force impulse image to evaluate liver fibrosis in the patients with non-alcoholic fatty liver disease

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Nonalcoholic fatty liver disease (NAFLD) is an important cause of chronic liver injury in many countries around the world. The degree of liver fibrosis must be estimated to determine the prognosis, surveillance, and optimal treatment for NAFLD. Liver biopsy is the gold standard for the diagnosis of NAFLD but its disadvantages, including the risk of complications, and sampling bias. The acoustic radiation force impulse (ARFI) elastography can be applied for the diagnosis of liver fibrosis and cirrhosis. ARFI imaging in the assessment of NAFLD related hepatic fibrosis is promising.

Methods:
All of the 56 patients NAFLD or NASH proven by histopathology, 5 patients were excluded out because of ARFI failure (no successful ARFI measurement after 10 attempts and IQR greater than 30%). Total 51 patients (35 males, 16 female) were investigated in this study. ARFI measurement was performed with curved-array transducer (6CI probe) of the Siemens ACUSON S2000 ultrasound system (Siemens Medical Solutions, Erlangen, Germany).

Results:
The mean measurement of stage F0 was 1.15, F1: 1.16, F2: 1.39 and F3:1.33. The P value between ARFI median value and fibrosis stage was non-significant (P= 0.13).

Conclusion:
ARFI elastography seem to be non-significant for NAFLD Taiwanese with non-cirrhotic fibrosis stage (F03).
According to World Health Organization, 100 million population are suffering from liver cirrhosis. Also approximately 88 thousand people die due to liver disease in every year. Liver plays an important role in the metabolism of trace elements. Liver disease is leading to lose the trace elements metabolism and change in their levels. This has been reported to be highly sensitive and clinical important in the diagnosis of liver disease. The concentration of each trace element varies with different types of liver diseases because these elements may have a direct hepatic toxicity or may be decreased as a consequence of the impaired liver function. Trace element contents and their ratios are frequently reported to be good biomarkers for diagnosis of various cancers. Hair analysis is a simple diagnostic technique, based on the idea that hair provides vital clues about nutritional imbalances elsewhere in the body.

The objectives of this study are to evaluate the hair some trace elements (Cu, Zn) in patients with liver cirrhosis and to assess their association with severity of the disease. Forty sex cirrhotic subjects of either sex ranging in age from 20–69 years were included in the study, and the results were compared with 11 age- and sex-matched healthy control subjects.

This study was conducted at The Third State Central Hospital, Gastroenterology Department. Scalp hair samples were collected from 46 cirrhotic patients (24 males and 22 females), age ranged between 20 to 69 years and 11 healthy subjects (6 males and 5 females), age ranged between 24 to 65 years. Trace elements in scalp hair were analyzed by total reflection x-ray fluorescence method. Statistical analysis was performed using SPSS.

Forty sex clinically diagnosed patients of cirrhosis (male 52 % and female 48 %) were included in the study, and results were compared with age- and sex-matched 11 normal healthy control subjects (56% male and 46% female). Trace elements (hair Cu, Zn) were evaluated in all the subjects. Hair copper was found significantly increased in patients with liver cirrhosis as compared to the control group (mean±SD, 98.7±196.7 vs 4.93±4.48 mg/kg, p<0.001). Whereas hair zinc levels were significantly decreased in cirrhotics as compared to controls (mean±SD, 214.7±88.7 vs 498.66±163.97 mg/kg, p<0.001). Cirrhotic patients (n=46) were further segregated into three groups according to the severity of liver disease as assessed by the Child-Pugh classification as Child A (mild), B (moderate), and C (severe). According to Child-Pugh Score, out of 46 cirrhotic patients, 8(17.3 %) belonged to Child A, 16 (34.7 %) to Child B, and 22 (47.8 %) in Child C category. Trace elements (Cu, Zn) were assessed for severity of liver cirrhosis. The concentration of zinc decreased with severity of liver disease, and the mean level difference was statistically significantly (p<0.001).

Trace element abnormalities may reflect the condition of liverdysfunction. Our results suggest that liver dysfunction may alter the metabolism of trace elements. Our study shows that micronutrient status in liver cirrhosis correlates well with severity of liver cirrhosis. Micronutrient supplementation in liver cirrhotic patients may prevent progression of disease and development of complications; however, further research needs to increase number of participants.
Liver stiffness measurement using elastography point quantification

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Background: Chronic viral hepatitis is the most important public health problems and main cause of liver fibrosis. Progressive hepatic fibrosis will gradually lead to liver cirrhosis, hepato-cellular carcinoma and liver failure and deaths. Study of liver fibrosis is becomes an essential issue of prevention, prognosis and radical treatment plan. The evaluation of liver fibrosis using ultrasound based-electrographic shear wave elastography (SWE) with elastography point quantification (ElastPQ) is a modern non-invasive method.

This study is aimed to evaluate diagnostic value of SWE with ElastPQ feature of liver fibrosis.

Methods: A total of 110 patients with chronic viral (B,C and D) infection and 50 healthy controls were involved. Quantitative evaluation of LS was performed by Philips iU 22 ultrasound system with ElastPQ using convex transducer C5-1.

Results:
In HBV patients: no fibrosis F0 score 7, mean liver stiffness 3.1±0.28 kPa, mild liver fibrosis F1 26, mean LS 4.9±0.90 kPa, F2 score 4, mean LS 8.0±0.56 kPa, F3 score 3, mean LS 11.0±0.83 kPa, and F4 score liver cirrhosis 2, mean LS 17±4.3 kPa, respectively. In patients HCV; F0 score 5, mean LS 3.2±0.08 kPa, F1-36, mean LS 5.0±0.94 kPa, F2 score-10 mean LS 8.1±0.90 kPa, F3-10, mean LS 10.9±1.03kPa, and F4 score 5, mean LS 15.9±2.8kPa, respectively. In patients with HBV, HDV; F0 score-1, liver stiffness was 3.2kPa, F1-13, mean LS 4.9±0.72 kPa, F2 score 2, mean LS 8.0±0.56kPa, F3 score, 10.8kPa, F4 score 1, LS was 20.1kPa.

Conclusions:
Shear wave elastography with elastography point quantification technique is a reliable that can to detect of the earlier fibrosis stage in chronic viral hepatitis patients. ElastPQ SWE method is an optimal to monitor liver tissue stiffness in patients with chronic liver diseases.

Non-invasive test for estimation of liver fibrosis

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In 2015 the digestive disorders were the second leading cause of morbidity among Mongolian population. The observed mortality from cancer in 2013 was 23.4% including liver cancer which is the first most common cause of cancer death. Furthermore, the digestive disease related death accounts for 4.7% of all mortality. Recently many noninvasive markers for assessing liver fibrosis have been developed, and they are frequently used in clinical practice. FIB4 index had a predictive value to confirm the existence of significant fibrosis with a specificity of 74% and a sensitivity of 70% and APRI score had a sensitivity of 89% and a specificity of 75%.

Methods:

Cross sectional study was carried out. A total of 120 patients were enrolled in this study including 40 healthy individuals, 40 patients with chronic viral liver disease and 40 patients with alcoholic liver disease. Complete blood count (PLT), biochemistry (AST, ALT), abdominal ultrasonography were performed. APRI, FIB-4 scores were calculated and compared with the results of the laboratory tests.

A total of 120 patients were enrolled in this study; 40% of patients were males. Their mean age was 43.43±10.93 years. Liver fibrosis stages that are determined by APRI score: F0-1 mild fibrosis accounts for 54.3%, F2-3 moderate fibrosis 40.6%, F4-cirrhosis 11.5%; by FIB4 score: 62.8% was in F0-1, 20.3% was in F2-3, 11.5% was in F4 stage among alcoholic liver disease group. In viral disease group liver fibrosis stages that were evaluated by APRI score were 36.2%-F0-1 mild fibrosis, 32.4%-F2-3 moderate fibrosis, 31.4%-F4 severe fibrosis. Statistically significant difference were observed between alcoholic liver disease and viral liver disease groups in liver fibrosis stages that was determined with APRI score (p<0.05).

In the abdominal ultrasonography increased echogenicity in alcohol group 32.5%, in virus group 52.5%, hepatomegaly in alcohol group 43.6%, vena portae dilated in alcohol group 8.3%, in virus group 10.6%, splenomegaly in alcohol group 14.1%, in virus group 20.1%, splenic vein dilated on alcohol group 20.3%, in virus group 14.75%. Alcohol and viral hepatitis abdominal ultrasonography is a statistically significant difference.

In the present study, we found a statistically significant negative correlation between FIB4 score and platelet count, moderate negative correlation between FIB4 score, and albumin, total protein level, weak correlation between alkaline phosphatase, GGT, total bilirubin levels and FIB4 score (p<0.05). APRI correlated significantly with AST and ALT levels, whereas platelet count, total protein albumin levels demonstrated moderate negative correlation with APRI scores (p<0.05).

The APRI F2-3, the FIB4 F0-1 and F4 scores showed high sensitivity for the diagnosis of alcohol related liver fibrosis. The FIB4 F2-3, F4 score showed high sensitivity for the diagnosis of virus related liver fibrosis. These measures also demonstrated significant correlation with the stage of liver fibrosis in patients with viral hepatitis.

For non-invasive diagnosis of liver fibrosis F2-3, using FIB4 was related to necroinflammation, F4 was related with necroinflammation, cholestasis, hypersplenism, liver failure syndromes.
Background and objective: Besifovir is an acyclic nucleotide phosphonate known to be effective in hepatitis B virus (HBV) DNA suppression for both treatment-naïve and lamivudine-resistant chronic HBV infection in preliminary studies; we assessed the safety and efficacy of besifovir comparing with tenofovir in treatment-naïve chronic hepatitis B patients.

Methods: A total of 193 patients were randomly received besifovir dipivoxil 150 mg or tenofovir disoproxil fumarate 300mg. Eligible subjects were patients with chronic HBV infection. We measured the proportion of patients who had HBV DNA less than 69 IU/mL at week 48 as the primary efficacy endpoint. Key secondary endpoints were histological response (i.e., a reduction in the Knodell necroinflammation score of 2 or more points without worsening fibrosis), serum HBV, DNA reduction, and liver function tests. Also, bone mineral density (BMD) and renal parameters were evaluated.

Results: The proportion of patients who achieved primary endpoint of HBV DNA (<69 IU/mL) at week 48 were 85.33% and 88.75% among those to be non-inferior to tenofovir (lower limit of 95% CI for the treatment difference = -0.14). Histological improvement of 29 patients who underwent liver biopsy was evaluated, and we found that significantly more patients treated with besifovir had improved histological response.
than those treated with tenofovir (77.78% vs 36.36%, p=0.0482). None of the patients had resistant to mutations or increase in serum creatinine > 0.5 mg/dl from baseline. Patients who received besifovir had smaller decrease in BMD during 48 weeks than that of tenofovir (besifovir -0.02±0.44, tenofovir -0.10±0.86, p= 0.0248). There was no adverse drug reaction leading the patients to withdrawal.

This phase 3 study demonstrated that besifovir had comparable efficacy and safety profile to tenofovir in the treatment of treatment-naïve chronic hepatitis B patients. Besifovir showed better profile than tenofovir in both histological response and bone loss. An open-label extension study is ongoing with besifovir to investigate long-term efficacy and safety.

Conclusions:
This phase 3 study demonstrated that besifovir had comparable efficacy and safety profile to tenofovir in the treatment of treatment-naïve chronic hepatitis B patients. Besifovir showed better profile than tenofovir in both histological response and bone loss. An open-label extension study is ongoing with besifovir to investigate long-term efficacy and safety.

Background:
Mongolia has the world's highest rate of liver cancer mortality—prevalence of chronic viral hepatitis B (HBV), C (HCV), and D (HDV) in Mongolia are at an endemic level and constitute the main cause for Mongolia’s world-leading liver cancer mortality rate. To eliminate HCV, to control HBV and HDV and to reduce liver cirrhosis and hepatocellular carcinoma mortalities significantly in Mongolia, it is critically important to identify every individual’s viral hepatitis infection status. Therefore, the aim of this pilot study was to determine feasibility of conducting general population hepatitis screening in Mongolia. In other words, every Mongolian would be screened for HBV and HCV infection and register the viral hepatitis infection status of every individual into a central database, which is the main goal of the Screening Campaign of the Hepatitis Prevention, Control, and Elimination Program in Mongolia.

Methods:
In this study, HBV and HCV screening campaign was launched through 40 primary (38) and secondary (2) public healthcare facilities in Ulaanbaatar as an early onset of the Hepatitis Screening Campaign. Under
this pilot project, 13,664 individuals were screened for HBsAg and anti-HCV using onsite, rapid diagnostic
tests (CTK Biotech, San Diego, USA) within 4 months.

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Out of 13,664 individuals screened within this pilot project, 1,859 or 13.6% were anti-HCV positive, while
1,165 or 8.5% were HBsAg positive. In total, there were 3,024 or 22.13% of all screened individuals had viral
hepatitis infections. Irrespective of hepatitis infection status, every individual was registered into the
Mongolian Electronic Health Records (MeHR) System.

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With this pilot project, we demonstrated that it is certainly possible to screen every Mongolian for HBV,
HCV infections utilizing the public healthcare infrastructure, registering infection status of individuals into
an electronic registration system that would enable people with chronic infections to proper care. Based
on this pilot project, we estimate that the entire Mongolian population screening can be completed within
2 years. Finally, it should be noted that as a result of this pilot project, the Government of Mongolia
officially adopted a plan on April 12, 2017 to conduct a decentralized general population hepatitis
screening in cooperation with all relevant public and private stakeholders. Under this plan, every citizen 40
or older will be screened for hepatitis B and C in 2017, and people who are 15-40 years old will be
screened in 2018, yielding a great example of science leading to a real action on ground in the fight of
eliminating hepatitis.

PE-083

Results of using kanema in clinic

Ulzmaa. G¹, Zorig. T², Tserendash. B³, Batbold. B²

Objective:
Results of using Kanema in clinic.

Methods:
We did the treatment Kanema, made by Medical Korea Co., Ltd, preparation of 25 mg dyphenil, dimethyl
bicarboxylat (DDB). We use Kanema in the 50 patients with chronic hepatitis Band C, liver cirrhosis. First
we gave 2 tablets 3 times a day for a month then we gave 1 tablet 3 times a day for 2 months. We
researched some biochemical indicators before the treatment and after 30 and 60, 90 days of the
treatment.

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Decreased biochemical indicator such as bilirubin, AST, ALT, LGH, GGT after treatment with chronic
hepatitis and no effect protein and albumin in patients who have chronic hepatitis. Decreased biochemical
indicator such as bilirubin, AST, ALT, total protein, albumin in patients who have liver cirrhosis. Bur
increased LGH, GGT in patients who have liver cirrhosis.

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It is very useful to use Kanema in Chronic Hepatitis B and it is increasing result of using Kanema with
preparation Glicovit (preparation of amino acid and protein)
N. Tuvshinbayar, R. Baigal, B. Gegeebadrakh

Among the estimated 185 million people in the world who have chronic hepatitis C virus (HCV) infection, and in the Mongolian who have chronic hepatitis C virus (HCV) infection approximately 95-98% have the genotype 1 strain of the virus. Genotype 1 infection has been historically difficult to treat, but multiple recent studies have shown treatment results greater than high in these genotype 1b patients using well-tolerated, all-oral regimens consisting of new direct-acting antiviral agents.

Define the effects of ledipasvir/sofosbuvir treatment on patients with HCV genotype 1b infection.

In this randomized, open-label trial, all the patients received a fixed-dose combination tablet containing 90 mg of ledipasvir and 400 mg of sofosbuvir, administered orally once daily. We enrolled 118 treatment-naive and 6 treatment-experienced, totally 124 patients who took ledipasvir/sofosbuvir during the period from January 2016 to March 2016. The primary end point was a sustained virologic response at 12 and 24 weeks after the end of therapy. The primary efficacy end point was the rate of sustained virologic response, defined as the absence of quantifiable HCV RNA in serum (<25 IU per milliliter), at 12 weeks after the end of therapy among all patients who underwent randomization and were treated. Secondary end points included the rate of sustained virologic response at 24 weeks after the end of treatment.

The SVR12 and SVR24 rates were greater than 95% and no differences were observed in treatment-naive versus treatment-experienced patients. Among patients who received ledipasvir—sofosbuvir alone, the incidence of adverse events was higher in the 24-week group than in the 12-week group (98.6% vs. 97.8%). A total of 2 patients had virologic relapse after finishing treatment.
Spontaneous bacterial peritonitis (SBP) is one of the most serious complications of liver cirrhosis. Mainstay of treatment for SBP is use of proper antibiotics. Although, several antibiotics including cefotaxime, ceftriaxone, or ciprofloxacin has been used as the first-line treatments, it is unclear which of these drug is still effective. Our aim of study is to compare the efficacy of the three current antibiotics for the treatment of SBP in patients with liver cirrhosis.

Methods:
This is multicenter prospective randomized controlled trial. The primary hypothesis is that the efficacy of all the antibiotics will not significantly different. This is a non-inferiority trial, and 87 patients for each group were needed to demonstrate it. Inclusion criteria were 16-70 years old liver cirrhosis patients with ascites, of which PMN cell count >250/mm³. Exclusion criteria were (1) allergic to 3rd generation cephalosporin or quinelone, (2) antibiotics within 2 weeks, (3) open abdominal surgery within 4 weeks, (4) evidence of secondary peritonitis, intraabdominal hemorrhage, pancreatitis, Tb peritonitis, or peritoneal carcinomatosis, (5) hepatocellular carcinoma with portal vein thrombosis, (6) pregnant woman, (7) HIV positivity. Antibiotics were randomly assigned to the patients after receiving informed consents. We performed follow-up paracentesis at 48 hours (day 2) and 120 hours (day 5) after administration of antibiotics, and assessed the resolution rates: decrease of PMN cell count in the ascetic fluid less than <250/mm³ was primary efficacy endpoint.

Results:
This study was conducted at 9 tertiary hospitals of 7 university between June 2007 and June 2016. A total of 261 liver cirrhosis patients who developed SBP were enrolled. The resolution rate of SBP at day 5 were 69.1%, 76.2%, and 76.1% in cefotaxime, ceftriaxone, and ciprofloxacin group. The efficacy was not different between the groups (P = 0.565). The early resolution rate of SBP at 48 hours were 54.5%, 53.1% (p = 0.946). The 1 month mortality after SBP was similar between the groups. (p = 0.628) MELD score (OR 1.074, CI 1.009-1.144, p = 0.026) and the resolution at day 5 (OR 0.251, CI 0.094-0.670, p = 0.006) were significant factors for survival.

Conclusions:
The efficacy of primary antibiotics such as cefotaxime, ceftriaxone, and ciprofloxacin were not significantly different. It is considered that these antibiotics are still efficacious. MELD score and the resolution of SBP at day 5 were most important factors for short term survival.

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In Mongolia, since 2016 for the treatment of HCV infection was started to use sofosbuvir/ledipasvir, which were imported from many foreign companies. The Mongolian Em Impex Concern is importing the Ledvir (sofosbuvir 90mg/ledipasvir 400 mg) from Mylan Company. We aimed to study the treatment result of Ledvir (sofosbuvir 90mg/ledipasvir 400 mg).
The cohort study was done for 24 patients, who were treated with Ledvir (sofosbuvir 90mg/ledipasvir 400 mg) during 12 weeks for patients with chronic hepatitis C, 24 weeks- with cirrhosis. The selection of patients was depended on clinical, biochemical, virological and APRI, FIB4 indicators. The treatment result was assessed at the end of 12th and 24th week of the treatment. The SPSS21 program was used for the data analysis.

**Results:**

The average age of patients was 48.5±23.5 and 62.5% of them - a man, 37.5% - female. 75% of patients had a chronic hepatitis C without cirrhosis, the cirrhosis with Child-Turcotte-Pugh score (CTP) A and B were occurred in 20.8% and 4.2%, separately. In all patients were detected 1b genotype of HCV. The ALT (99±65) and AST(55.65±39.55) were decreased (ALT 21.5±10.5 and AST20.5±10.5; p<0.01) at 12th week of the treatment among the patients with chronic hepatitis. In patients with cirrhosis the ALT(99.5±60.5) and AST(79.45±42.55) were decreased at 24th week after the treatment till ALT26.5±19.5 and AST22±10 (p<0.01). End of the treatment the APRI was decreased from 1.174±0.663 to 0.277±0.13, the FIB4 – from 2.95±1.77 to 1.96±1.3 (p<0.01). The platelet cell was increased from 186±88 to 243±76.5 in patients with chronic hepatitis (p<0.01), in patients with cirrhosis were analyzed 144±32 and 177±21 (p<0.01). End of the treatment at the 12th and 24th week was not detected the HCV-RNA in all patients. The side effect was noticed in 20.5% of all patients.

**Conclusion:**

Ledvir (sofosbuvir 90mg/ledipasvir 400 mg) of Mylan is effective for the treatment of HCV infection.

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**Prevalence of hepatitis B virus carriage among 4-6 year-old children in Mongolia**

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Hepatitis B virus infection (HBV) is widespread and highly endemic in Mongolia. Consequently, complications of HBV including liver cirrhosis and primary hepatocellular carcinoma, are crucial public health problems in the country.

The main goal of this study is to determine the prevalence of HBsAg among children aged 4-6 years old in Mongolia.

A nationwide population-based cross-sectional survey was conducted in order to determine the prevalence of HBsAg carriage among children of Mongolia. Serum samples of children were tested for HBsAg using “The Abbott Determine HBsAg”, Japan. N = 5894 children were participated in the survey out of 6380 selected (response rate 92.38%) children (2839 girls and 3055 boys) who were aged 4-6 years (mean age: 4.96±0.8). Prevalence of HBsAg carriage was 0.53% (n=31) that was 0.59% and 0.45% among boys and girls, respectively (p>0.05). The positivity rate of HBsAg in Metropolitan cities, Province center, and Rural areas were 0.33% (8/2423), 0.34% (3/882), and 0.77% (20/2589) respectively (p<0.05). The prevalence of HBsAg carriage of 4, 5 and 6 year-old children were 0.34%, 0.66%, and 0.56% respectively, without statistical significance.
The prevalence of HBsAg carriage among children is decreased to 0.53% due to the national immunization program. The prevalence of HBsAg carriage was higher in rural Soums (0.77%) compared to Metropolitan cities (0.33%) and Province centers (0.34%). No significant differences in the HBsAg carriage rate were found by age (p=0.359) and sex (p=0.444) whereas prevalence of HBsAg carriage was higher in the Western and Eastern regions.

Prevalence of hepatitis B and C virus infection among street urchins
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Background and objective: Viral hepatitis are the most common cause of serious health problems such as liver cirrhosis and hepatocellular carcinoma (HCC). Hepatitis A (HAV) is thought to spread by the faecal-oral route, while Hepatitis B (HBV) and Hepatitis C (HCV) are mostly transmitted vertically during childhood. In our study, we aimed to determine the seroprevalence of HAV, HBV, and HCV among street urchins who were admitted to outpatient clinics.

Methods: Between April 2014 and April 2016, the data of 187 street urchins aged between 6-18 years included in the study. Serum samples from children were asseyed for HAV antibody IgG (anti-HAV IgG), HBV surface antigen (HBsAg), antibodies against HBV surface antigen (anti-HBs), antibodies against HBV core antigen (anti-HBc total), HCV antibody (anti-HCV) using the ELISA (Enzyme-Linked Immunosorbent Assay) method.

Results: HBsAg, anti-HBs, anti-HBc total data of 156 patients (83.4%); anti-HCV data of 114 patients (60.9%); and HAV IgG data of 86 patients (45.9%) were reached. 53.4% of patients were female, with a mean age of 12.52 years among all patients. The data for the study are summarized in table 1.

<table>
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<td>Percent (%)</td>
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Discussion and Conclusion: The socioeconomic and sociocultural levels of street urchins are generally low. Due to inability of these children to access primary health care services and the inability to follow HBV vaccination regularly, HBsAg seroprevalence of street children is thought to be higher than in other children and anti-HBs positivity is thought to be less. In recent studies, the seroprevalence of HBsAg in a group aged 0-18 years in Turkey was found to be in the range of 3-12%. In our study, on the contrary this rate was observed to be similar than that reported in Turkey. In studies conducted in Turkey, Anti-HCV positivity was 0-1% and Anti-HAV IgG
positivity was 34% in the pediatric age group. As a result of our study, anti-HCV seroprevalence in street children was similar to that in Turkey, and anti-HAV IgG positivity was more frequent. Hepatitis A seropositivity may be explained by the fact that life in the streets is not a matter of cleaning habits. According to the results, if the street children get into the national HAV and HBV vaccination schedule, hepatitis infections and their complications may be prevented.
The aim of this study is to evaluate the care cascade of HCV-infected persons, particularly an efficacy and safety of an all-oral regimen for the treatment of patients with genotype 1b (GT1b) hepatitis C virus in a single center, prospective, observational cohort study.

Persons were enrolled who screened for HCV –antibody in our hospital, and also patients who initiated HCV treatment with posttreatment follow-up. According to the regional and WHO standards of care, HCV RNA – PCR were performed in HCV seropositive persons, then persons with HCV RNA positive were illegible for HCV –antiviral DAA treatment. Information was collected from the medical records and abstracted into a centralized data. Demographic, clinical, adverse events (AEs) and virological data are collected throughout treatment and follow-up. Patients received 8-week, 12-week, and 24-week Ledipasvir (LDV)/ Sofosbuvir (SOF) 90/400 mg/day treatment. CBC, biochemistry and serum HCV-RNA PCR measured at week 4, at treatment completion day and at week 12 after treatment completion. This analysis assessed sustained virologic response (HCV RNA PCR not detected [<10 IU/mL]) at post-treatment week 12 (SVR12).

Eight thousand fifteen persons involved for HCV-antibody screening and 1353 (16.8%) of them were HCV seropositivity. 603 persons from HCV infected took HCV RNA-PCR test and HCV RNA detected in 322 (53.3%) persons. One hundred twenty patients were enrolled for HCV treatment evaluation: mean (SD) age 52.7 (range 18-87) years; 73 female; HCV G1 – 100%; baseline HCV-RNA was below 6.000.000 IU/ml in 90,8%. HBV coinfection noted in 6, HBV and HDV triple infection in 2 patients; HCV treatment-experienced 14.3 %. Patients with chronic hepatitis were 81, liver cirrhosis - 32 and hepatocellular carcinoma -7. Treatments authorized were: LED/SOF 8 weeks (n = 13; 10.8 %); 12 weeks (n = 93; 77.5 %); and 24 weeks (n = 14; 10.8 %). None of AEs noted in 68.3 %, and common adverse effect was headache (10%).
SVR was achieved in 116 (96.7%) overall, Non-Response 3 (2.5%), and Relapse - 1(0.8%). Achieving SVR were 98.8% in hepatitis group, 93.8% in liver cirrhosis group, and 85.7% in hepatocellular carcinoma group ($\chi^2 = 8.348$, $p>0.08$). Liver cirrhosis and hepatocellular carcinoma were the significant predictor for treatment non response as 2(6.2%) and 1(14.3%) patients all 3 non-response (NR) in liver cirrhosis and hepatocellular carcinoma group, respectively. Only 1 case of relapse (R) noted who presented in hepatitis group. All patients with NR and R outcome received 12-week treatment regimen.

Prevalence of HCV seropositivity among hospital based population was 16.8%. High SVR12 rates (96.7 %) were achieved during treatment with the LED/SOF regimen in Mongolian patients with GT1 infection, including those with liver cirrhosis and hepatocellular carcinoma. All range of health care service include HCV screening, detection and treatment are available in Mongolia.
We have conducted data on Hepatitis diseases and its counter-reaction in Mongolia between 1951 and 2016 using retrospective cohort. We have analysed on morbidity of Hepatitis B, C, D and its statistical data.

Between 1992-1997 ninety-six children who have had acute Hepatitis D virus at Clinic of Infectious Diseases. The thirty nine patients (40.6%) were diagnosed with anti-HDV IgM, HBsAg, anti-HBc IgM, HBeAg as coinfection, while remains (59.4%) were diagnosed with anti-HDV IgM, HBsAg as super infection. 5.9% of patients were diagnosed with HBV/HDV, 0.8% of patients were diagnosed with HBV/HCV as co-infection in 2007.

There were 653 patients underwent at Clinic of Infectious Diseases in 2015. The ninety-six (14.8%) patients were positive anti-HCV, while 324 (49.6%) patients were positive HBsAg. 460 patients who underwent at Clinic of Infectious Diseases in 2016. The sixty-seven (14.6%) patients were positive anti-HCV, while 279 (60.6%) patients were positive HBsAg. The nine patients (3.2%) were positive anti-HDV IgM, HBsAg (as HDV super infection) while a patient (0.6%) were positive anti-HBc IgM (+), HBeAg (as HDV co-infection).

Conclusions:
1. The patients aged between 15 and 34 and patients aged between 25 and 54 are commonly infected by HBV and HCV infections respectively.
2. 240 patients (71.2%) with HBV and 57 (54.4 %) patients with HCV have common anamnesis as who have had any risk of treatment and service.
3. The patient with HCV requires between 11-30 million tugriks for its treatment, which leads on financial crisis of the patient.

In Mongolia, especially in Ulaanbaatar the outbreak of viral hepatitis A was reported every two years before 2012. The routine vaccination for viral hepatitis A was implemented beginning in 2012 with 2 doses of vaccine for children between the ages of 14 months and 2 years. A cute viral hepatitis, which occurs in Ulaanbaatar, is referred to the National Center for Communicable Diseases. Since 2014 the National Center of Communicable Diseases has detected the anti-HEV-IgM for patients, who were referred to the hospital with jaundice. We were instructed to study the morbidity of HAV and HEV infection in Mongolia in years (2014-2016).

We actively studied the morbidity of HAV and HEV infection, which were registered in National Center for Communicable Diseases during 2014-2016. In 2011 the National Center for Communicable Diseases registered 3786 case of viral hepatitis A. In subsequent years the numbers of cases were: Year 2012- 2128 cases, Year 2013-692 cases, Year 2014-113-cases, Year 2015-24 cases and Year 2016-10 cases. After vaccination of viral hepatitis A the morbidity of viral hepatitis A decreased 5-300 times than in previous years. The average age of patients with HAV
infection was 11±8.2 years. In 5.2% of all acute HAV infections were confirmed by detection a HAV-IgM. During the years of 2014-2016 years 130 cases of HEV infection were registered 17 cases in 2014, 106 cases in 2015 and 7 cases in 2016. The average age of patients was 31±11.9 years, 60% of them male, 40% female. 24.6% of patients used water from the central water supply or their apartment. 75.4% living in houses and used potable portable water. 27.7% of patients had contact with a jaundice patient. 72.3% the source of contact was certain. The HEV infection was confirmed by anti-HEV-IgM.

Conclusion: The effectiveness of viral hepatitis A vaccine is high in Ulaanbaatar. The HEV infection is occurring in adults.

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Mongolia has one of the highest prevalence of hepatitis B and C viruses in the world. An estimated 400,000 people live with chronic viral hepatitis in Mongolia. Despite the high prevalence, most people are unaware of viral hepatitis and its health consequences. In addition, over 70% of the infected people are not aware of their infection status. In this study, we evaluated the current understanding about transmission routes of hepatitis B and C viruses, as well as overall awareness within the general population in Mongolia.

A cross-sectional questionnaire to evaluate the knowledge and awareness about transmission and prevention of hepatitis B and C among the Mongolian population was administered from January to October of 2015. The questionnaire included questions ranging from basic demographics information to modes of transmission and viral hepatitis prevention. Participation was voluntary and without compensation. The participants were asked to answer each question with “true”, “false”, or “do not know”. After completion of the questionnaire, descriptive statistics were used to describe the respondents’ demographic characteristics. Statistical Package for Social Sciences (SPSS) was used for data analysis.

A total of 2,257 respondents including 1,441 (65.45%) females, 816 (36.1%) from both urban and rural areas were enrolled in this study. Nearly 60% of study participants correctly identified that blood transfusion, needle injection, and medical procedures are major infection pathways for viral hepatitis. However, still around 32% of study subjects did not know these transmission routes, whereas small percentage ~3% of participants had incorrect information. Interestingly, 53.5% of participants did not know that HBV could transmit sexually, while 40.6% correctly responded to this question, indicating a big gap of knowledge and awareness. 11% and 44.1% of participants correctly responded that shaking hands or kissing do not put them in risk for hepatitis infection, whereas 51% and 47.1% of participants still did not know the answer. The study results also showed that knowledge and awareness of study subjects about viral hepatitis transmission is positively correlated with their education level (p<0.005).
In certain areas, Mongolian public do have relatively good knowledge and awareness. This may stem from the fact that viral hepatitis is known as “the needle infection disease” in Mongolia. On the contrary, sexual transmission of hepatitis B is not well known among the Mongolian public. At the same time, Mongolian population is still not aware that viral hepatitis can lead to liver cirrhosis, hepatocellular carcinoma and death. This finding is particularly puzzling, since Mongolia has the highest liver cancer mortality rate in the world—nearly eight times the world average and this fact is constantly circulated in both traditional and social media. The results of this study provided the baseline data for the Prevention Campaign of the Hepatitis Prevention, Control, and Elimination Program in Mongolia, and similar study will be conducted in 2018 to assess an effectiveness of the Prevention Campaign in improving the knowledge and awareness of hepatitis among the Mongolian population.

**Markers of viral hepatitis in the sera of HIV-positive prisoners**

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High prevalence of HIV and viral hepatitis co-infection are determined by common transmission routes of these viruses. Prisoners are known as high risk group and former prisoners are playing a significant role in spreading of these infections in common population. This study assessed the prevalence of HCV, HBV, HGV, HDV, TTV markers among HIV-positive persons in a prison.

Cross-section epidemiologic study was conducted in Irkutsk region. In 2016 83 males 20-59 age old with laboratory confirmed HIV-infection were selected. All of them had two or more previous convictions. Sera were tested by ELISA for presence of HBsAg and IgG antibodies to HCV, HGV, HDV, TTV. HGV RNA и TTV DNA were detected in real time PCR. Human DNA samples from sera were tested for polymorphisms of IFN L3 gene (rs 12979860 и rs 8099917) using single nucleotide genotypic assay.

Antibodies to HCV were detected in most of HIV-positive prisoners – 91.6% (85.7 - 97.5). Antibodies to other viruses were detected as frequently as: HGV – 44.6% (34- 55.2), HDV - в 4.8% (0.3 – 9.3), TTV в 65% (54.8 – 75.2). Positive findings of HbsAg composed 20.5% (11.9 – 29.1), PHK HGV - 12% (5 - 19), ДНК TTV – 43.4% (32.8- 54). Mixed of antibodies to several viruses also were detected in many cases: HCV+ HGV в 43.4% (32.8 - 54), TTV+HGV - в 31.3% (21.3 - 41.3). Frequency of HCV antibody findings within prisoners groups with different genotypes in relation with probability of spontaneous clearance from HCV , composed 66,7% (55,8 - 77,6) for TT genotype and 47.8% (35,8 — 64,2) for CC genotype. According with published data, frequency of HCV antibodies composed near 2% in common population in Irkutsk region (S. I. Malov, 2017).

The results of this study demonstrated very high prevalence of haemo-contact viral hepatitis, especially HCV, among HIV-positive prisoners in Irkutsk region. No relations were detected between HCV antibody prevalence and frequency of CC и TT polymorphisms of interferon Lambla 3 gene among HIV-positive persons ( χ² = 0,5 and 0.1 correspondently, p >0,05).
Ledipasvir/sofosbuvir for 12 weeks is safe and effective in patients with chronic hepatitis C and hepatitis B co-infection: A phase 3 study in Taiwan


¹C, j, h, h, N, fk, j, h, h

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Patients co-infected with hepatitis C virus (HCV) and hepatitis B virus (HBV) have more rapid liver disease progression and worse outcomes than patients mono-infected with either HBV or HCV. Taiwan has among the highest prevalence of chronic HCV/HBV co-infection in Southeast Asia. In Taiwan the standard of care for HCV/HBV co-infection is peginterferon plus ribavirin for 24 or 48 weeks. This study evaluated the safety and efficacy of an all-oral treatment with ledipasvir (LDV)/sofosbuvir (SOF) for 12 weeks in patients with chronic HCV and HBV co-infection.

Patients with or without compensated cirrhosis chronically infected with HCV genotype (GT) 1 or GT2 and HBV (positive for serum HBsAg) not currently receiving HBV treatment were enrolled into this open-label ongoing study to receive LDV 90 mg/SOF 400 mg (once daily) for 12 weeks. The primary efficacy endpoint is SVR12. HBV DNA was monitored at all study visits during treatment and it will be monitored for 2 years post-treatment. The start of HBV treatment was based on the APASL guidelines.

A total of 111 patients (68 [61%] with GT1 and 43 [39%] with GT2) were enrolled and treated. The majority were female (62%), treatment naïve (67%), and non-cirrhotic (85%), with a mean age of 55 years (range 32-76) and mean BMI of 24.5 kg/m² (range 17.3-33.8). All but one were HBeAg negative. Mean (range) baseline HBV DNA was 2.1 log₁₀ IU/mL (1.3-5.8). SVR4 was 100% (111/111). Full SVR12 data will be presented. The mean change in HBV DNA ranged from -0.06 log₁₀ IU/mL at week 1 to +0.49 log₁₀ IU/mL at follow-up visit 4; HBV DNA kinetics are shown in Figure1. 60 (54%) patients had an increase in HBV DNA kinetics > 10 x BL or became HBV DNA ≥ LLOQ, No patients had ALT ≥ 2 x baseline. To date no patients have started HBV therapy. No patients discontinued treatment due to adverse events (Aes). Three patients had serious Aes. One each of optic neuritis, post procedural bleeding and duodenal ulcer bleeding; none was considered drug related. The most common Aes reported (≥5% of patients) were headache, upper respiratory infection, and fatigue.

In patients with chronic HCV/HBV infection, LDV/SOF for 12 weeks resulted in an SVR4 rate of 100%. Although most patients had an increase in HBV DNA during treatment, this was not associated with ALT elevations ≥2 x baseline, and no patients started HBV therapy to date. This all-oral, interferon-free regimen was well tolerated, supporting its potential as a treatment option for HCV/HBV co-infected patients.
Expression of gene profiles on hepatocellular carcinoma cells with different intracellular hepatitis C viral load

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Objectives: The different hepatitis C virus (HCV) replication has been reported among individual hepatocytes in chronic HCV infection by identifying hepatocytes with different HCV RNA levels. With the previously established fluorescence-activated cell sorting (FACS) protocol, we want to study the effects of different intracellular viral loads in HCV-infected cells. The present study aimed to further study the gene expression on different hepatocellular carcinoma (HCC) cells with different HCV viral load.

Methods: The JFH1-EYFP viral fluorescence intensity was used to sort the high and low viral load cells after 5 days infection in vitro which has been shown in our previous study that infected cells efficiently and accurately discriminated between high- and low-viral load cell populations. The next generation sequence-RNA sequence was used to clarify the mRNA and miRNA gene network between HCV-high and HCV-low infected cells of the HCC cell line. Venn diagram summarizing the probe sets that were differentially expressing between the Huh7.5.1 versus each differential viral load cell population and miRDB and miRTar databases were used to predict HVL and LVL/S2 unique miRNA target genes.

Results: By analyzing the NGS dataset and miRNA microarray dataset, of the significant transcripts, three miRNA were unique for the LVL/S2 cells and nine miRNA unique for the HVL. Twenty-three miRNA were common for all 3 viral load groups. We verified them by q-PCR and data confirmed the array data expression level. We found that high viral loads were associated with cell inflammation- and cell death-associated pathway; and the low viral loads were associated with many stress response- and cell adhesion molecule (CAMs) related genes.

Conclusions: We have demonstrated that different gene network between HCV-high and HCV-low infected cells in JFH1-EYFP infectious cells exists with the established cell sorting protocol. Our results may provide a broader gene regulation map between high and low viral load cell populations.

Boceprevir-based triple therapy to rescue HCV genotype 1/HBV dually infected patients refractory to peginterferon plus Ribavirin combination therapy in Taiwan

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Background:
Recent study showed that the risk of HCC incidence is even higher among HBV/HCV co-infected persons than those with HBV or HCV mono-infection. Previous studies showed that the PEG-IFN/RBV has been effective in the treatment of HCV-dominant, treatment-naïve patients with HCV/HBV dual infections. The aim of this study is to explore the safety and efficacy of boceprevir-based triple therapy to rescue HCV genotype 1/ HBV dually infected Taiwanese patients refractory to peginterferon plus ribavirin combination therapy.

Methods:
We enrolled 12 eligible patients who agree to join this clinical trial from Kaohsiung Medical University Hospital (KMUH) and National Taiwan University Hospital (NTUH) from March 2014 to December 2014. These 12 patients were classified according to if patients suffered from liver cirrhosis and the response of previous PEG-INF/RBV therapy (relapse, partial responder, and null responder.)

Result:
7 relapses and 5 null responders were among these 12 subjects. 8 male and 10 HCV genotype 1b subjects were enrolled in this study. No event of death happened in this study, and 2 SEA were noted. Anemia (1/6), but no neutropenia and thrombocytopenia were also noted. Until now 1 of 3 relapse reach to the SVR 12, and percentage of undetectable HCV RNA more than 70% during period of therapy regimen.

Conclusions:
Even this study is in progress, we think that from the preliminary data, boceprevir-based triple therapy to rescue HCV genotype 1/HBV dually infected patients refractory to peginterferon plus ribavirin combination therapy is effective and under consideration.

The risk of hepatitis B virus reactivation is considerably high during sorafenib therapy in patients with advanced hepatocellular carcinoma


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Chronic hepatitis B (CHB) is the most leading cause of development of hepatocellular carcinoma (HCC). It has been reported that reactivation of hepatitis B virus (HBV) frequently occur during HCC treatment such as transarterial chemoembolization, resection, or radiotherapy. Reactivation of HBV replication in and prognosis of HBV-related HCC. In advanced HCC patients, soranefrib is the treatment of choice. However, the effect of soranefrib on the replication of HBV remains unknown. Here in, we evaluated the rate of HBV reactivation during soranefrib therapy in CHB patients with advanced HCC.

We retrospectively reviewed 277 advanced HCC patients at three hospitals affiliated with Korea University. Among the, 213 patients were HBsAg positive. One hundred seventy one received antiviral therapy before initiation of soranefrib therapy, and 42 patients were treatment naïve with regard to anti-HBV therapy.
Among the 42 treatment naïve CHB patients with advanced HCC, 7 patients who received soranefrib less than 4 weeks and 10 patients who had not follow-up HBV DNA value were excluded. Finally, 25 patients were analyzed. HBV reactivation were defined as increase of HBV DNA > 10 times of baselines or ≥2,000 IU/mL in patients with baselines HBV DNA < 200 IU/mL. Factors associated with patient’s survival were also analyzed.

Results:
Mean age was 53.8±11.42 and 80% were male. All patients were Barceloan Clinic of Liver Cancer Stage C. Mean baseline HBV DNA level was 2.69±0.29 log IU/mL. Median survival was 9.57 months. No patients received locoregional or systemic therapy other than sorafenib. During the sorafenib therapy, HBV reactivation developed in 24% at 12 weeks, 32% at 24 weeks and 36% at 48 weeks. The probability of reactivation rate was considerably higher in these patients than in those receiving antiviral therapy (p<0.001). We also analyzed factors associated with patients' survival. In patients who didn’t take antiviral agents, the length of sorafenib therapy (HR 0.375, C.I. 0.169-0.834, p = 0.016) and age (HR 1.077, C.I. 1.002-1.157, p = 0.045) was significantly associated with patients’ survival. Patients taking sorafenib for a longer period tended to reactive HBV.

Conclusions:
The risk of HBV reactivation is high in CHB patients receiving sorafenib due to advanced HCC. It would be necessary to administer pre-emptive antiviral therapy before sorafenib initiation.

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Since sorafenib was approved in patients with advanced hepatocellular carcinoma (HCC), a variety of novel compounds have been able to indicate survival benefits in sorafenib failure/refactory patients. Regorafenib has been investigated for its efficacy and safety as a second-line treatment in a phase III trial (RESORCE trial). However, this trial designed based on stringent enrollment criteria and included patients who had a radiological progression during sorafenib treatment and tolerability of dosage of sorafenib 400 mg or more. The goal of this study was to assess characteristics of advanced HCC patients who had possibility to convert to 2nd line treatment especially regorafenib from sorafenib in the field practice.

Patients with HCC treated with sorafenib as first line systemic therapy were retrospectively analyzed based on the database of Chiba University Hospital. This study included only Child-Pugh A and ECOG-PS ≤1 patients. We defined 2nd line candidate patients as maintaining Child-Pugh A and ECOG-PS ≤1 at the time of radiological progression or treatment discontinuation according to adverse events. We also defined regorafenib candidate patients as follows: (1) continued sorafenib at the time of radiological progression, (2) maintaining Child-Pugh A and ECOG-PS ≤1 at the time of radiological progression, and (3) continuing sorafenib 400 mg or more without intolerable adverse events more than 21 days of last 28 days of treatment.
Of 185 patients, 127 patients (69%) were Child-Pugh score 5 and 112 patients (61%) were ECOG-PS 0. Fifty-five patients (30%) had macrovascular invasion and 83 patients (45%) had extrahepatic metastasis. Majority of patients (161 patients, 87%) continued sorafenib until radiological progression. Overall survival and time to progression were 14.8 months (12.3-17.3 months) and 2.9 months (2.3-3.5 months), respectively. According to our definition, 130 patients (70.1%) and 69 patients (37.3%) were candidate of 2nd line treatment and regorafenib. Child-Pugh score 5 and ECOG-PS 0 at the time of starting sorafenib were significantly higher than both 2nd line treatment and regorafenib candidate patients. In multivariate analysis, those two factors had significantly high odd ratio of conversion from sorafenib in HCC patients.

Regorafenib candidate patients were not majority of sorafenib treated HCC patients. Patients who were Child-Pugh score 5 and ECOG-PS 0 patients seemed to be likely to convert to regorafenib from sorafenib.

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MHC class I chain-related A (MICA) genetic variants and its serum level (sMICA) were associated with hepatitis C virus (HCV) related hepatocellular carcinoma (HCC) in untreated cohorts. The dynamic changes of serial sMICA levels regarding anti-HCV treatment and consequent HCC development is elusive.

Single nucleotide polymorphism rs2596542 of MICA and serial sMICA levels were tested in chronic hepatitis C (CHC) patients with sustained virological response after antiviral treatment. Forty-two patients who developed HCC and another 84 age-, sex- and cirrhosis-propensity score matched non-HCC controls were compared. Serial sMICA levels were measured at three-time points: within 6 months of pretreatment (pre-sMICA), 6 months after the end of treatment (post-sMICA) and last visit before HCC occurrence or not (last-sMICA).

Compared to patients without HCC occurrence, those with HCC had lower platelet counts, higher levels of post-sMICA (197.4±398.0 pg/mL vs. 57.6±89.6 pg/mL, P=0.03) and last-sMICA (320.4±508.4 pg/mL vs. 37.7±140.2 pg/mL, P<0.001). Cox regression analysis revealed that last-sMICA is the only factor predictive of HCC development (hazard ratio [HR]/ 95 % confidence intervals [CI]: 2.27 (per 1 log pg/mL increase)/1.672-3.082, P<0.001) Patients without HCC had a significantly decreased trend of sMICA levels during follow-up (trend P=0.001). In contrast, HCC patients had an increased trend of sMICA levels (trend P=0.024). MICA rs2596542 GG genotype carriers without HCC had a significantly decreased trend of sMICA levels compared to HCC patients.
Serial sMICA levels could serve as a surrogate marker for HCC development in CHC patients with SVR. The clinical utility is restricted to MICA rs2596542 GG genotype carriers. CA (320.4±508.4 pg/mL vs. 37.7±140.2 pg/mL, P<0.001). Cox regression analysis revealed that last-sMICA is the only factor predictive of HCC development (hazard ratio [HR]/95% confidence intervals [CI.]): 2.27 (per 1 log pg/mL increase)/1.672-3.082, P<0.001). Patients without HCC had a significantly decreased trend of sMICA levels during follow-up (trend P=0.001). In contrast, HCC patients had an increased trend of sMICA levels (trend P=0.024). MICA rs2596542 GG genotype carriers without HCC had a significantly decreased trend of sMICA levels during follow-up (trend P<0.001). However, HCC patients who carried GG genotype had a substantially increased trend of sMICA levels (trend P=0.06). Nevertheless, both trends were not observed in A allele carriers with or without HCC development. t three-time points: within 6 months of pretreatment (pre-sMICA), 6 months after the end of treatment (post-sMICA) and last visit before HCC occurrence or not (last-sMICA).

**561**

**Antiviral therapy in patients with chronic hepatitis C related hepatocellular carcinoma**

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Advances in hepatitis C virus (HCV) treatment offer high sustained virologic response rates with minimal side-effects. However, benefits of eradicating HCV in hepatocellular carcinoma (HCC) patients whose life expectancies are hard to be determined after palliative therapy still needs to be assessed. This study sought to evaluate prognostic factors for survival in HCV related HCC patients that responded to the initial HCC therapy in order to speculate whether treating HCV would be beneficial in patients that received palliative therapy and showed response.

In this retrospective cohort study, the medical records of patients diagnosed and treated for HCV related HCC and seen at Yonsei University College of Medicine, Gangnam Severance Hospital, Seoul, Republic of Korea from January 2004 to January 2016 were reviewed. Among 181 patients with HCV related HCC, 16 patients had HCV treated before the diagnosis of HCC. From 165 HCV related HCC patients whose HCV infection had never been treated, 115 patients that showed complete (CR) or partial response (PR) to the initial HCC treatment, were included in this study. Among 115 patients, 80.0% (92/115) of them received palliative treatment. After univariable and multivariable analysis, receiving HCV treatment (HR, 0.0149 [95% CI, 0.035-0.633]; P=0.010), showing CR to the initial HCC treatment rather than PR (HR. 0.450 [95% CI, 0.263-0.771]; P=0.004) increased the survival rate, and having advanced liver fibrosis, determined by FIB-4 index during the follow-up, increased the risk and decreased the survival (HR, 4.324 [95% CI, 1.235-15.136]; P=0.022). From 115 patients, 16 patients were eventually treatment for HCV. The median time from HCC diagnosis to initiation of HCV treatment
was 14.5 months (range 3-97 months). All 16 patients had at least 3 months of HCC remission period before HCV treatment. Fifteen patient achieved SVR (15/16, 93.8%).

Although treating HCV in HCC patient that undergo non-curative HCC treatment is still detectable, this study results carefully suggest that HCV related HCC patients that responded to the initial HCC therapy might benefit from HCV treatment regardless of HCC treatment modality.

PE-101
Low albumin and high FIB-4 serum model for predicting high mortality of hepatocellular carcinoma after surgical resection
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Hepatocellular carcinoma (HCC) is the leading cause of cancer deaths worldwide. Resection is the first-line of treatment for patients with early tumors. Two noninvasive methods, including Child-Turcotte-Pugh (CTP) and Model for End-stage Liver Disease (MELD) score, have often been used to evaluate liver function in place of the liver biopsy. We wished to build a simple model of serum markers in replace of complex CTP or MELD scores for predicting mortality after resection.

A total of 812 HCC patients receiving tumor resection were consecutively examined in central and south Taiwan from 2000 to 2015. A hospital-based cohort was designed to collect serum markers to further assess liver functions. We used the ROC curve method to find the optimal cutoff value of significant serum factors and evaluated them by the Kaplan-Meier method. Finally, we used multivariate Cox Proportional Hazard Regression to adjust for the other confounding factors.

Besides traditional factors and tumor characteristics, serum markers, albumin and fibrosis index (FIB4) were independent factors for predicting mortality. Albumin <4g/dL or FIB-4 ≥3 index was strongly associated with higher mortality. There was about a two-fold higher risk of death in patients with at least one serum risk compared with those in patients without any risk factors (adjusted p value=0.014; HR=2.01). It is interesting that albumin<4g/dL or FIB-4≥3 enabled better sensitivity when CTP or MELD class supported a better specificity for predicting all-cause mortality.

Patients with at least one risk factor (albumin<4g/dL or FIB-4≥3) had high mortality after resection. The serum combination with higher sensitivity might be a good predictive model as CTP or MELD with higher specificity for death, which indicated the important value of albumin and FIB-4 in the follow-up.
Hepatocellular carcinoma (HCC) is the 16th overall cause of deaths globally, and one of the most frequent malignancy leading to cancer-related death. Namely, majority of patients diagnosed as HCC proceed to end-of-life stage in their clinical courses. However, impact of survival after moving onto end-of-life care has been still controversial.

Between January 2008 to July 2015, 440 patients were consecutively decided to discontinue any active treatments against HCC in multidisciplinary team of our department and agreed with patients to proceed end-of-life care (i.e. Patients receive only best supportive care). We retrospectively analyzed the impact of survival from the date of starting end-of-life care. Tumor factors and status of sarcopenia (measured of skeletal muscle by computed tomography [CT] scan) were evaluated by dynamic enhanced CT within one month before the date of baseline.

We enrolled 223 patients who were able to evaluate all variables in this study. Majority of patients were male (75.8%), hepatitis C virus-antibody positive (57.8%), Child-Pugh B or C (90.6%), and alpha-fetoprotein (AFP) 400ng/mL or higher (56.1%). The median time from initial diagnosis to starting end-of-life care and the time from starting end-of-life to death were 24.2 months and 1.7 months, respectively. In multivariate analysis, Child-Pugh C, ECOG-PS >2, presence of sarcopenia, intrahepatic tumor burden (>50%), and AFP>400 ng/mL were independent prognosis factors of survival after moving onto the end-of-life care in patients with HCC.

Two parameter indicating physical status (ECOG-PS and presence of sarcopenia) as well as liver function and tumor status contributed prognostic after starting the end-of-life care in patients with HCC. These results seem to be useful in that an objective parameter such as presence of sarcopenia evaluated by CT scan might help to make a decision regarding the end-of-life care.
Background and objective: Metabolomics investigates metabolic changes in biological systems and provides mechanistic insights into the course of a disease. This study assessed the metabolomic profile of serum to identify metabolic changes related to the development of hepatocellular carcinoma (HCC) in hepatitis B virus (HBV) carriers.

Methods: We conducted a nested case-control study in a cohort of male Taiwan's civil servants recruited in 1989-1992 and followed till 2010. Among 2878 hepatitis B surface antigen-positive men, prediagnostic serum samples were from 121 incident cases of HCC and 121 controls. Cases and controls were matched for age and time of blood collection. Liquid chromatography-quadrupole time-of flight mass spectrometry coupled with pattern recognition method and system analysis was performed to evaluate metabolomic profile changes and pathways related to the development of HCC.

Results: Of 167 metabolites obtained, 13 revealed at least a borderline significant association with future HCC event (p = 0.0567 - p < 0.0001). Eight top significant metabolites (false discovery rate [FDR] q<0.05) include bile acid metabolism products, amino acid (tyrosine), and nucleobases/nucleosides (hypoxanthine, inosine, and uridine). Compared with controls, tyrosine and bile acid metabolism products were increased in cases, whereas nucleobases/nucleosides were decreased. Principal component analysis (PCA) on all differential metabolites identified two metabolite factors for which the estimated principal component scores showed significant and opposing associations with HCC risk after adjustment for demographics, serum alanine aminotransferase, and HBV DNA and genotype. The adjusted-odds ratios of HCC for highest vs lowest quartiles were 10.74 (95% CI: 2.07-55.88) for factor 1 (which mainly contains metabolites in bile acid biosynthesis) and 0.16 (95% CI: 0.03-0.88) for factor 2 (which mainly contains nucleobases/nucleosides). Pathway enrichment analysis on the combination of differential metabolites in bile acid biosynthesis (FDR q = 0.0435), which is consistent with the PCA results.

Conclusions: The findings indicate the potential key role of metabolic alterations in bile acid biosynthesis early in the pathogenesis of HBV-related HCC, and suggest new light for developing strategies to prevent HCC.

Prediction of hepatitis B virus reactivation in lymphoma patients with resolved hepatitis B virus infection who received rituximab-containing chemotherapy: the roles of antiHBc/antiHBs quantification


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Prophylactic antiviral therapy was recommended to prevent HBV reactivation for lymphoma patients with resolved HBV infection who received rituximab-containing chemotherapy. This study sought to identify high-risk patients by measuring baseline levels of serum anti-HBc and HBs.
We prospectively followed the HBV DNA levels of 197 lymphoma patients with resolved HBV infection who received rituximab-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone)-based chemotherapy and started antiviral therapy upon HBV reactivation, defined as a greater than 10-fold increase in HBV DNA compared with previous nadir levels (www.clinicaltrial.gov/identifier: NCT 00931229). Anti-HBc and anti-HBs levels were measured by double antigen sandwich immunoassay and enzyme immunoassay. Receiver operating characteristic curve analysis was used to determine optimal baseline anti-HBc/HBs levels for prediction of HBV reactivation.

Results:
The median baseline anti-HBc and anti-HBs levels were 4.25 IU/mL (range 0.23-191.86) and 72.3 mIU/mL (range 0-12513.5) for the 192 patients with enough serum samples for analysis. High anti-HBc (>=6.41 IU/mL) an low anti-HBs (<56.48 mIU/mL) were significantly associated with high risk of HBV reactivation (odds ratio 5.42, and 8.87, respectively, p<0.001). The cumulative incidence of HBV reactivation at 15 monts was 45.8% (95% CI 27.3-64.2) for patients with both high anti-HBc and low anti-HBs baseline (36 of 192 patients) and 3.0% - 9.6% in other patients (p<0.001). HBV reactivation, when considered as a timedependent covariate, independently predicted inferior overall survival (HR 2.41, 95% C.I. 1.15-5.05, p=0.02).

Conclusions:
Baseline anti-HBc/qnti-HBs levels may predict HBV reactivations. Efficacy of prophylactic antiviral therapy for the long-term clinical outcome should be explored. (supported by grant PH-102PP-11, PH-103-PP-11 from National Health Research Institutes, Taiwan).

Strong correlation of hepatitis C virus prevalence with HCC mortality rate

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Mongolia has the highest mortality rate of hepatocellular carcinoma (HCC) in the world that is nearly eight times higher than the world average. Among all 21 Mongolian provinces, Uvs has the fourth highest incidence and mortality due to HCC. The mortality rate of HCC increased 91% from 39.8 per 100 000 people in 2003 to 75.9 per 100 000 people in 2015. Geographically, Uvs province is located on the northwestern border of Mongolia, about 830 miles away from Ulaanbaatar, the capital city. About 400 thousand people are chronically infected with hepatitis B (HBV) or C virus (HCV) in Mongolia and at risk to develop into liver cirrhosis and HCC. In the current study, we intended to determine the prevalence of hepatitis B (HBsAg), hepatitis C (anti-HCV) and their correlation with HCC mortality rate in Uvs Province, Mongolia.
A total of 15’893 people or nearly 30% of the adult population in Uvs province, (6082 male, mean age 40.52±12.97) participated in hepatitis screening activities between March and May of 2016. HBsAg and anti-HCV in participant’s peripheral blood were detected using on-site HBsAg and anti-HCV rapid tests that are based on lateral immunoassay technology (CTK Biotech Inc, San Diego, USA). All participants completed a structured demographic questionnaire. The Pearson’s correlation test was used to determine a correlation between the prevalence of HBsAg, anti-HCV and the actual HCC mortalities in Uvs Province between 2003 and 2015. Data from participants were entered and analyzed using the Statistical Package for Social Science (SPSS) version 17.0 (SPSS, Chicago, IL, USA).

Results:
Overall, 1,569 (9.87%) and 1,511 (9.51%) people were positive for HBsAg and anti-HCV, respectively (Fig. 1). 73 (0.46%) people were positive for both HbsAg and anti-HCV. The average HCC mortality rate between 2003 and 2015 was 64.06±12.72 per 100 000 population. By correlating the prevalence with the HCC mortality rate, the Pearson’s coefficients resulted at \( r=0.27 \) and \( r=0.63 \) for HBsAg and anti-HCV, respectively. For HBV/HCV dual infections, the correlation coefficient was \( r=0.52 \).
The mortality rates of HCC by counties of Uvs province (per 100 000 people). The star and rectangular shapes denote the prevalence in percentage of HBsAg and anti-HCV positivity in each county. Color coding shows the HCC mortality. Blue spots denote lakes in Uvs.

**Conclusions:**
HBV and HCV prevalences are at a similar level compared to recent nationwide prevalence studies among Mongolian adults (9.87% vs 11.1% for HBV and 9.51% vs 8.5% for HCV). HCV prevalence is strongly correlated with the HCC mortality in Uvs Province compared to the HBV prevalence, thus indicating that HCV contributes more to HCC mortalities compared to HBV.

095

**The risk of hepatocellular carcinoma (HCC) after Directly Acting Antiviral (DAA)**

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We present a patient with chronic hepatitis C who developed HCC despite sustained virological response and lack of cirrhosis.
63 years old women was diagnosed with chronic hepatitis C (genotype 1b, F1) in 2005. Before the treatment HCV RNA was 1845200 IU/mL. She completed a 12-week course of Ledipasvir 90mg/Sofosbuvir 400 mg treatment with sustained viologic response. At baseline and at the end of HCV treatment, computed tomography (CT) scan of abdomen excluded any lesions suspected for HCC. However, alpha-fetoprotein was 35 IU/mL before DAA treatment, increasing up to 152 IU/mL at week-44 of follow-up after the completion of therapy. Transaminase levels were not rising. She was found to have a 1.5 cm, no enhancing hepatic lesion at segment 8 on CT. The lesion was treated with radiofrequency ablation.

Our case suggests that the combination of SVR and less fibrosis may not be fully protective against HCC after DAA treatment. It also raises the issue of how to optimize HCC surveillance after the treatment. In our case, the increase of alpha-fetoprotein was the first signal. Mechanisms underlying the development of HCC among such patients are still not well-understood and need further investigations.
Our results implied that EHPC did not affect OS, but HCC-related survival was better in patients with EHPC. Based on these findings, the management of additional primary cancer is warranted.

Background and objective: Mongolia has the highest rate of mortality caused by liver cancer per 100,000 populations and this rate is eight times higher than the global average. In developing countries, more than 50 percent of liver cancer is caused by hepatitis C virus and the main cause of liver transplant is chronic viral infections, mainly caused by hepatitis C virus. Therefore, the measures such as early liver cancer detection and monitoring have been critical, and the need to determine risk factors, and preventive actions are emerging. The goal of our study was to determine the prevalence of hepatitis C virus and liver cancer marker levels among people aged 40-64 years of Bayanzurkh district, Ulaanbaatar city.

Methods: In this study, cross-sectional study a multi-stage sampling method was used for selecting people aged 40-64 of Bayanzurkh district, Ulaanbaatar city. The study was carried out between December, 2016 and March, 2017. Anti-HCV and liver cancer marker AFP was determined by chemiluminescence enzyme immunoassay method with fully Automated Immunoassay system HISCL-5000 of Sysmex. This study financially supported by Sysmex Corporation of Japan, Tottori University of Japan and Science Technology Foundation of MNUMS.

Results: In this study, a total of 293 people, aged between 40 and 64 years have been participated from Bayanzurkh district, Ulaanbaatar city. The estimation of prevalence of HCV carried out and the majority of the study participants (243) had anti-HCV-negative (82.9%) and anti-HCV-positive recorded in 50 people (17.1%). Anti-HCV-positive people were classified by age and gender as 9 people belong to 40-44 age groups (18%) and from them 4 were men (33.3%), 5 were female (12.3%) and 11 people in 45-49 (22%), from them 2 men (16.7%), female 9 (23.7%) and 16 people in 50-54 (32%) from which 3 men (25%), 13 female (34.2%), 9 people in 55-59 age group (18%), from which 1 man (8.3%), 8 female (21.1%) and 5 people in 60-64 age group (10%), from which 2 men (16.7%), 3 female (7.9%). There was no statistically significant difference between age and gender groups (p = 0.443).

Level of liver cancer marker AFP had been determined among participants and it had been detected in 3 people with Anti-HCV negative (1.3%) and in one patient with Anti-HCV positive (2.2%). This findings was
above the reference value of as AFP marker. There was no statistically significant difference between liver cancer marker AFP and anti-HCV (p= 0.527).

The prevalence of Hepatitis C virus infection was 17.1% among people aged 40-64 of Bayanzurkh district. High level of liver cancer marker AFP was recorded in 1.5% of participants.