Daily News

Modern Hepatology

25th Conference of the Asian Pacific Association for the Study of the Liver

The Japan Gastroenterological Endoscopy Society · The Japan Society for Portal Hypertension · The Japan Society of Hepatology · The Japanese Liver Transplantation Society · The Japanese Society of Gastroenterological Surgery · The Japanese Society of Gastroenterology · The Liver Cancer Study Group of Japan · The Organization of JDDW

Tokyo SUNDAY, 21 February 2016

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Today

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Produced by:
HEPATOLOGY DIGEST
www.ihepa.com:8088/pc/41/special/index.html
Editor-in-chief: Hui Zhuang

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Address from Imperial Highness Princess Tomohito of Mikasa

It gives me great pleasure that the 25th General Assembly of the Asian Pacific Association for the Study of the Liver (APASL) is being held for the first time in our capitol city of Tokyo, following Fukuoka in 2000 and Kyoto in 2007.

It is my hope that this meeting of 4000 researchers from 60 countries specializing in the treatments of liver disease under the main theme of Modern Hepatology, will take this opportunity to discuss and deliberate, from all angles from fundamental to clinical studies, a permanent cure for the liver disease.

As you well know, it is said that 75% of all liver disease ailments are found in Asia. I am very proud and grateful to APASL which is based here, together with AASLD of the United States and EASL of Europe, for their tireless efforts in the treatment and research of liver disease.

It was 30 years ago that a prominent medical doctor whom I highly respected said, of the many academic fields, the medical field is the only one not explicated. In the midst of research into diagnosis and treatment of illnesses, it is best, I believe, for individuals to be responsible and attentive to their own health. However, I truly feel that modern science and advanced technology and research, year after year, progress from one year to the next, in the span of two years, five years, have progressively made way to explicated diagnosis and treatments of diseases.

It is my hope that your research results will find hope and shed light to patients who are suffering and to show them a path to new life, and to prove to them that dreams can come true. My expectations from your studies and research are very high so that it will give strength to the patients. The patients, too, have high expectation from your research. I hope that you will be able to respond to their expectations. I am certain that your tireless efforts toward your research and studies and progressive results will give light and the will to live for these patients.

My dear Professor Omata, thank you for inviting me to address this meeting. I am grateful for this opportunity to meet with you all. I wish you all the best for a fruitful and successful meeting.

Masao Omata

Welcome Message

The Asian Pacific Association for the Study of the Liver (APASL) is one of the world's largest academic associations for Hepatology, founded in August 1978 (38 years ago) by Profs K Okuda and L Powell (Australia).

Originally, the APASL meeting was held biannually with hundreds of participants to discuss diagnosis and treatment of liver diseases including hepatitis, cirrhosis and hepatocellular carcinoma, more or less in closed manner.

However, the Asian Pacific region has the biggest number of patients, three-quarters of the world's total, suffering from liver diseases including Chronic Hepatitis, Cirrhosis and Hepatocellular Carcinoma due to HBV (Hepatitis B Virus) and HCV (Hepatitis C Virus) infections.

Because of the urgent and expansive need to offer better quality medical care for patients suffering from liver disease in Asia, and through the initiatives of Prof Shiv K. Sarin (India), myself and other leaders in this region, now, the APASL meeting has become an annual conference with more than 4000 experts from over 80 countries joining the meeting every year for the last 10 years.

Our organization also holds the Single Topic Conference (300-1100 participants each time) two to four times a year, with venues rotating all over in Asia, the last one at New Delhi in December, and publishes the international journal "Hepatology International" six times a year for education purposes.

The APASL Secretariat, located in Tokyo, also constantly provides up-to-date information through websites and E-News.

It is estimated that 75% of the world's liver patients exist in the Asian region. Based on this, in cooperation with AASLD (the American organization) and EASL (the European organization), APASL is a central academic society which plays a key role in treatment and the research of liver diseases throughout the world.

This Tokyo meeting will be the 25th APASL Annual Meeting, and will be held at the International Convention Center Pamir, Grand Prince Hotel New Takanawa from Feb 20 to 24, 2016. Previously, this meeting was held in Kyoto in 2007, but this is the first time Tokyo has hosted this annual gathering.

Under the theme of "Modern Hepatology", and under the President, Prof Osamu Yokosuka, the conference program was planned to contain up-to-date information and cutting edge lectures by eminent researchers, and to share state-of-the-art views and experiences regarding liver diseases towards the complete cure of liver diseases.

We believe and hope this meeting will help patients suffering most in Asia.

Masao Omata

Honorary President, The 25th Conference of the
Asian Pacific Association for the Study of the Liver

Osamu Yokosuka

Welcome Message

Dear Colleagues, It is a great pleasure for us to invite you to the 25th Asian Pacific Association for the Study of the Liver (APASL 2016) that will be held on February 20-24, 2016 in Tokyo, Japan. We are delighted to welcome you to the cultural, historical and scenic metropolis of Tokyo.

Under the theme of “Modern Hepatology”, the conference program will perform high quality content with full of maximum up-to-date information and cutting edge lectures by eminent researchers, to show mature, time-honored, well-established explanation of Hepatology in order to reconfirm their significance by scientists and clinicians for the achievement of better both basic and clinical practice.

The conference aims to raise awareness of the current status and future prospects to develop a better understanding of the roles, objectives and operations of the various institutions, academics, companies, associations, non-profit organizations, and other related sectors, to enhance communication and collaboration within all of us, and to deliver mutual benefits to the people in the Asian Pacific region, where liver disease has been one of the most common and serious problems.

As more than 4,000 delegates of experts from all over the world, more than 60 countries are expected to attend this Asian Pacific’s largest liver conference, we are sure that this is the perfect opportunity for those of us in the Asian Pacific region to share state-of-the-art views, values, experiences and practices regarding liver diseases, such as Viral Hepatitis, Liver Cancer, NASH, Liver Failure and other topics.

We are looking forward to welcoming you to Tokyo.

With warmest regards,

Osamu Yokosuka, MD., PhD.
President, The 25th Conference of the Asian Pacific Association for the Study of the Liver
Professor, Department of Gastroenterology and Nephrology, Chiba University Graduate School of Medicine

Welcome Message

Shiv Kumar Sarin

It is a matter of great pleasure that the Asian Pacific Association for the Study of the Liver (APASL) is holding its 25th meeting this year in Tokyo, Japan from February 20-24, 2016. It is a mattter of great pride for all of us that the Association and its Journal, the 'Hepatology International', have become symbols of excellence in liver diseases not only in Asia, but in the world. Liver diseases are more common in the Asian region and over the years, the clinicians and scientists from this region have given new protocols and science to the world.

It is in this context, the theme of the APASL 2016, "Modern Hepatology" is most befitting. The scientific committee needs to be congratulated for developing a very high quality program. The recent developments in each area are being covered by eminent hepatologists and researchers from all over the world.

More than 4,000 delegates from all over the world, from more than 60 countries, are expected to attend this Asian Pacific's largest liver conference. I believe that it would be a unique opportunity to learn from each other. I am delighted to note that special encouragement is being given to young investigators and basic researchers.

The Land of the Rising Sun, Japan, leads also in the tradition of hospitality and warmth. I am sure that the untiring efforts of the organizing teams under Prof. Yokosuka's dynamic leadership and Prof. Omata's patronage, would provide you with the most comprehensive and enjoyable academic event in the history of APASL.

On behalf of all the memebrs of the Steering Committee, I feel privileged to extend our full support and best wishes for a most successful and memorable APASL 2016.

Shiv Kumar Sarin
Chairman
Steering Committee, APASL

Welcome Message

Hiroshi Yatsuhashi

I am very pleased with Osamu Yokosuka, who is the President of this meeting, to be able to hold the 25th Asian Pacific Association for the Study of the Liver (APASL 2016) in Japan.

Looking back at previous APASL meetings in Japan, it was held in 2000 in Fukuoka by Dr Michitami Yano who is my teacher and it was held in Kyoto in 2007 by Prof. Masao Omata. We were able to be held in Tokyo to give a time of 8 years to give a cooperation of the member to be in this society.

We have gathered more than 1500 abstracts and presentations, the contents of which seems fresh and interesting and scholarly presentations have been prepared.

APASL is the largest of the hepatology societies of the Asia Pacific region, but has positioned itself as a very important society academically. It is also an important place to understand the liver disease patients and hepatology in each of the countries in the region.

Tokyo will host the Olympic Games in 2020, and the Japanese government and the Tokyo Metropolitan Government is already working on the preparation. Culturally, Tokyo also offers a charming city of food, fashion and architecture.

I am looking forward to seeing you and everyone in fascinating Tokyo.

Hiroshi Yatsuhashi
Vice President, The 25th Conference of the
Asian Pacific Association for the Study of the Liver

What to Watch Out for Today

Room 1ABCD		09:00 - 09:30	Opening Ceremony
Symposium 1. Barriers of HCV Treatment in Asian Pacific			
Room 1ABCD	09:30 - 09:50	Three Decades of Advances in Nucleotide Antivirals: from Research to Expanding Access	John C. Martin
Room 1ABCD	09:50 - 10:10	Barriers of HCV Treatment in Asia Pacific	Masao Omata
Symposium 2. APASL Guideline in HCV Treatment			
Room 1ABCD	14:15 - 14:35	APASL HCV and Transplantation	Geoffrey McCaughan
Symposium 3. HCV Treatment in Special Situation			
Room 1ABCD	15:50 - 16:10	Unmet Need for the Patients with Chronic Hepatitis C	Michael P. Manns
Room 1ABCD	16:10 - 16:30	Clinical Outcomes of Anti Hepatitis C Therapy	Massimo Colombo
Room 1ABCD	16:30 - 16:50	Challenges and Prospects of HCV Therapy Beyond the DAAs	T. Jake Liang

Reality or Dream: to Eradicate Hepatitis C and Hepatitis B

Eugene R. Schiff

"It has been estimated that once treatment programs get going, it will probably be thirty years and you could eradicate this disease."

Since almost all HCV infections could be cured by currently available oral direct-acting antivirals, could we expect an opportunity for the eradication of HCV worldwide? In an interview with APASL Daily, Professor Eugene R. Schiff, Schiff Center for Liver Diseases, University of Miami Miller School of Medicine, Miami, USA told us that we could expect the eradication of HCV but it would be over a thirty-year period. Because there is no vaccine for hepatitis C, it would mean treating everyone. Of course we can never get rid of every last case but we could get it where it is really very well contained. Something that is analogous to that was polio and the polio vaccine.

Eradication of HCV would be dependent for the large part on access: access to someone who is going to test and that means getting to a facility or service; and access to the drugs, which is limited by cost.

As far as access to a diagnosis, there are a lot of things that are being developed that may have a place in facilitating this. One is called point-of-care testing. The other issue is the access to the drug and that is variable. There are regions that are being used to demonstrate that HCV can be eradicated from that region where the resources do not otherwise exist. Prof. Schiff gave 3 examples of such regions - Egypt, the country of Georgia and Mongolia. For example, 15% of the population in Egypt is hepatitis C positive and disproportionately genotype 4. They obtained drug (a nucleotide polymerase inhibitor, sofosbuvir) at a much-reduced cost from one of the major manufacturers, Gilead. The cost of the course of the nucleotide polymerase inhibitor from Gilead for the patients in Egypt was $900. They coupled that with an NS5A inhibitor made by a company in San Francisco called Presidio. It is not licensed for use in the United States but now Egyptian interests own a significant proportion of the company. It is now been administered very effectively in Egypt. That program may well come close to eliminating HCV in Egypt over the next five or six years.

Prof. Schiff said, "In general, we are going to start to see more people being diagnosed and more people being treated. In some of these countries, drugs that are not licensed in the United States are being used that might be considered "counterfeit", but if they are effective and safe then fine. .I think we will see these drugs become much more widely available and more affordable. The talk I am giving at APASL is related to this in part. In Japan, one of the most common liver diseases is chronic hepatitis C. It is disproportionately genotype 1b. Now that these drugs are available, they are producing cure rates >95% on finite therapy. "

"Even when the cures for hepatitis C increase, they are going to have a significant component of patients who will need to be followed because of the advanced liver disease and cirrhosis that gives rise to hepatocellular carcinoma despite the eradication of HCV."

However, the question there might be, what is the future of hepatology going to be because a large part of the discipline currently focuses on hepatitis C? If we start with HCV itself, we know (particularly in Japan where the epidemic started well before that in the United States) that there is significantly more cirrhosis and cancer of the liver in their population related to HCV. Even when the cures for hepatitis C increase, they are going to have a significant component of patients who will need to be followed because of the advanced liver disease and cirrhosis that gives rise to hepatocellular carcinoma despite the eradication of HCV. Where there is advanced cirrhosis, the complications of cirrhosis need to be managed even though the underlying cause has been stopped.

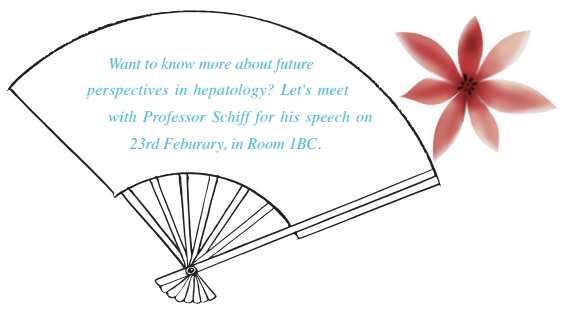
" The problem with HBV is that, unlike what we see with HCV, in the majority of cases, therapy is not finite."

When asked about the future of treatment of hepatitis B, Prof. Schiff thought it was particularly relevant to Asia. The predominant hepatitis in South-east Asia or sub-Sahara Africa is HBV. In those regions in particular, HBV has been transmitted in the past from mother to newborn (perinatal or vertical transmission). Right now, there is underway around the world, universal vaccination against hepatitis B. There is a long way to go in some of these countries particularly in Africa, but when the newborn is vaccinated against HBV, even though the mother is positive, infection in the infant can be prevented.

For those already with hepatitis B, treatment has come a long way. There are some similarities with HCV in that these are very effective pills. The first-line drugs are nucleotide and nucleoside analogs (entecavir and tenofovir from Bristol-Meyers Squibb and Gilead respectively). These pills can render a person with HBV negative for virus in their blood (i.e. HBV DNA-negative) and that returns liver chemistry to normal and histology reversal just as with HCV. Where there is fibrosis without advanced cirrhosis, removing the virus allows the fibrosis to regress over time. When the underlying inflammation that causes fibrosis is removed, there is no new fibrosis and there will be regression of existing fibrosis. The problem with HBV is that, unlike what we see with HCV, in the majority of cases, therapy is not finite. Even though the medications we have are very effective in stopping the progression to cirrhosis and reducing the risk for cancer of the liver, they have to be given continuously. When therapy is stopped, in most cases, it recurs. HCV can be cured with finite treatment, but that is not true with HBV in the vast majority of cases.

" The point is that for HBV, the new advance will be to accomplish finite therapy - to be able to give it for a given period of time and to achieve cure. "

To Prof Schiff, the challenge for hepatology in the field of HBV is to produce drugs that will get rid of cccDNA from the nuclei of infected liver cells. Currently, giving medication gets rid of the virus circulating in the blood, but because of the cccDNA in the nuclei of the liver cells, when therapy is stopped, the virus can begin replicating again. In people who appear to have recovered from HBV, even where HBsAg-negative, the cccDNA will persist in the core nuclei so if immunosuppression occurs with drugs like rituximab for example, HBV will be reactivated. The point is that for HBV, the new advance will be to accomplish finite therapy - to be able to give it for a given period of time and to achieve cure. We cannot do that now. We can achieve some good outcomes, but we can't cure it. Because patients need to stay on therapy indefinitely, cost and compliance come into play. The promising drugs are those that are focusing on cccDNA, but they are not there yet.



Barriers of HCV Treatment in the Asian Pacific Region

Today, four leading hepatologists from US, Japan, China and India, providing different perspectives, will discuss the challenges facing their fields in the Asia-Pacific region. This session is chaired by Dr Shiv K. Sarin, and Drs John C. Martin, Lai Wei and Masao Omata will also give their insights on how to tackle HCV infection.

Advances in Nucleotide Antivirals

"The recent introduction of a variety of DAA agents makes HCV cure possible for a majority of patients and is stimulating the design of elimination strategies for particular genotypes and geographies."

Direct viral polymerase inhibitors, nucleoside analogues, such as acyclovir(HSV, VZV), gancyclovir(CMV) and zidovudine(HIV) have been the mainstay of antiviral therapy. Although these early generation nucleoside analogues brought some significant side effects and were not tolerated well, they prolonged the lives of many patients around the world.

For thirty years, nucleotides such as tenofovir DF (TDF) have been the predominant agent for chronic therapy of HIV and hepatitis B infection. Eighty percent of HIV patients, close to one million in total, have been treated with TDF in Western countries, and 8 million patients have received TDF-containing regimens in developing countries, due to ease of accessibility.

In the last two years, the nucleotide analogue sofosbuvir(SOF) has rocked the treatment world of HCV. It is a highly effective, well-tolerated, once-a-day oral drug with a minimal resistance profile.

Not only has SOF worked well in combination with interferon, ribavirin and other DAA agents, but it has also been formulated with ledipasvir for a single pill treatment regimen.

According to Dr. John C. Martin, "As of September 2015, over 600,000 HCV infected patients have initiated treatment with SOF-containing regimens".

The key to solving the accessibility issue was to follow the precedent of TDF, to implement a generic access program.

45 years experience

"Recent and remarkable progress in the development of oral drugs has made it possible to eradicate HCV infection from all of my patients."

The biggest patient population worldwide suffering liver diseases is in Asian Pacific regions. These diseases include Chronic Hepatitis, Cirrhosis and Hepatocellular Carcinoma due to HBV (Hepatitis B Virus) and HCV (Hepatitis C Virus) infections.

Although, Some Asian countries have more patients suffering from HBV related disorders, whereas a country like Japan has a very different demographic and clinical feature whereby 70-80% of hepatocellular carcinomas are HCV-related.

"Of course the cost (of the new drugs) can be the barrier in the Asian-Pacific region. But it is an insidious disease and because there are no symptoms, patients come to the clinic at a very late stage. When patients had jaundice, bleeding appeared." Says Dr. Masau Omata.

"So the screening, or inefficient screening could be a barrier too", stresses Dr Omata.

In this symposium, Dr. Omata will address the issues of HCV treatment in Asia, based upon his experience for the last 45 years.

1% vs. 10 million in China

"More than 200,000 new cases of HCV were reported to China CDC in 2013"

Compared to the higher prevalence rate of HBV infection, the 1% HCV infection rate in China has usually not been paid as much attention as HBV. A recent public survey found that only 1% of the general public have some knowledge about HCV transmission and prevention.

Currently, Peg-Interferon/Ribavirin(Peg-IFN/RBV) is still the standard treatment regimen in China, with SVR rate ranging from 44-83% according to clinical study results.

According to Dr. Lai Wei, there are barriers from patients, as well as from health providers. From the patients' side, lack of awareness, low treatment efficacy, and HCV treatment affordability and treatment compliance and adherence all contribute to patients' long-term commitment to treatment. The lack of referral to specialists is the physicians barrier.

The high cost of the treatment, low reimbursement for lab tests and limited insurance may deter patients from commencing treatment

Because of the big population base in China, the 1% sero-prevalence means there are 10 million individuals suffering HCV infection, which is a strikingly big figure. HCV should be a key focus in China too.

Improved outcome of Decompensated Cirrhosis

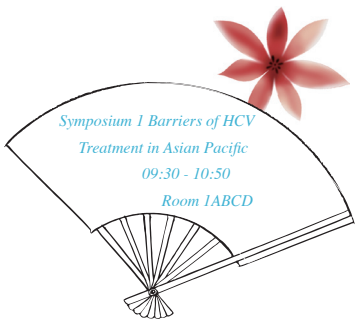
"The introduction of DAAs, including sofosbuvir (SOF), simeprevir, ledipasvir (LDV) and daclatasvir (DCV) has helped improve outcomes."

Before the introduction of DAAs, the treatment protocols and options for patients infected with HCV and having decompensated cirrhosis were limited and prognosis was very poor. The introduction of DAAs, including sofosbuvir (SOF), simeprevir, ledipasvir (LDV) and daclatasvir (DCV) has helped improve the outcome.

As shown by the results of SOLAR-1 and SOLAR-2 studies, genotype 1/4 HCV infected patients with Child B or C cirrhosis treated by LDV (SOF)+ribavirin(RBV) for 12-24 weeks, 575/627(92%) subjects achieved SVR12. Of the 250 decompensated patients who achieved SVR12, 60% (150) had an improvement in MELD scores. Similar data was shown in the ELECTRON-2 study and other studies. Although real life data demonstrates a higher relapse rate, SVR is often associated with a significant improvement in Child's and MELD score.

Newer drug combinations, like SOFO/Velpatasvir, Grazoprevir (MK-5172)/Elbasvir (EBR) and Abbvie 3D regimens have shown an improved SVR but raised some safety concerns with certain regimens.

Dr Sarin stresses that "though safe and effective in improving clinical state and outcomes, the DAAS should be used by experts in patients with DC as this group has a rapidly progressive disease, often with high bilirubin and renal impairment."



Different Role of Liver Biopsy between Hepatitis B and C

Hiroshi Yatsuhashi

A liver biopsy is needed for the patients with chronic hepatitis B, because it is difficult to decide prognosis and treatment policy in the patients whose complete viral clearance is difficult.

1 APASL Daily: The first time the APASL conference came to Japan was in 2000 in Fukuoka with your teacher, Dr. Michitami Yano, as the President. Now it's the third time APASL has been held in Japan and the former student has today become the Vice-president and committee member. What's your feeling about the development of APASL, also about the development of hepatology in Japan?

Prof. Yatsuhashi: As there are many viral hepatitis patients present in the Asian region, I perform clinical work and research of viral hepatitis under the guidance of Dr. Yano who is a my teacher. I have a great interest in the epidemiology, patients background, natural course and anti-viral effect. I have a great interest in what are the differences and similarities between Japan and Asian countries. I am very pleased that we have been able to hold this third APASL in Japan.

2 APASL Daily: Non-invasive diagnosis of liver fibrosis has been widely used in these years. Do we still need liver biopsy to stage and score the disease in liver? When is a liver biopsy unavoidable in your opinion?

Prof. Yatsuhashi: Non-invasive examination of the liver such as FibroScan or several kinds of simple blood tests (FIB-4, APRI-score and M2BPGi etc.) are used in Japan. Among such circumstances, I also think that liver biopsy is needed for the patients with AIH, PBC or NASH because such liver disease needs histological findings as diagnostic criteria. However, I have a special thought with respect to the hepatitis B. I think a liver biopsy is needed for the patients with chronic hepatitis B, because it is difficult to decide prognosis and treatment policy in the patients whose complete viral clearance is difficult. In contrast, the significance of liver biopsy is becoming smaller in chronic hepatitis C patients due to the viral clearance that can be achieved these days.

3 APASL Daily: Standardization will be helpful and perhaps is necessary to improve the diagnostic performance of non-invasive diagnostic methods. But the related guidelines seem scarce. Will APASL develop a guideline on noninvasive diagnosis?

Prof. Yatsuhashi: I feel there may be difficulty in establishing guidelines on noninvasive diagnosis in APASL at this time. This is not just limited to guidelines on non-invasive diagnosis because across medical care, economics, society and culture, there is a large variation across the Asia-Pacific countries. The features of the Asia-Pacific countries is that they have a diversity that is not uniform. By to develop with future work through APASL, consensus among the countries with such diversity will be established in the near future.

4 APASL Daily: You're very famous for research on the various types of hepatitis. Which kind of hepatitis is the gravest in Japan now?

Prof. Yatsuhashi: Among the five types of hepatitis virus, hepatitis C virus has the strongest impact in Japan. It is apparent that liver cancer as the terminal stage of liver disease is closely associated with hepatitis C infection in Japan. Future interest in liver disease in Japan may move from hepatitis C to hepatitis B.

5 APASL Daily: HBV genotypes differ in their clinical manifestations and responses to therapy. The Japanese have been infected with genotypes B and C mainly. However, an article published in *J Gastroenterol Hepatol* by you and your colleagues mentioned that the distribution of genotype A had also increased. Will current therapy need adjustments?

Prof. Yatsuhashi: Indeed, the main genotypes of hepatitis B virus in Japan are genotype B and C until now. As we have reported in *GUT* 2011, genotype A infection is increasing in Japan. This is due to globalization. This phenomenon is expected to further accelerate. Of course, I also think that it is necessary that treatment guidelines adapt in Japan to the presence of genotype A.

Unmet Need for the Patients with Chronic Hepatitis C

Michael P. Manns

Professor Michael P. Manns, Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Germany, is scheduled to speak on the Unmet Need for the Patients with Chronic Hepatitis C-including genotype 3, DAA resistance, HCV recurrent post transplantation, decompensated liver disease and renal insufficiency, etc.

Therapy for chronic hepatitis C virus (HCV) infection has been revolutionized due to interferon-free, all-oral combinations with direct acting antiviral agents (DAA) targeting the HCV protease, polymerase and NS5A protein. Sustained virological response (SVR) rates of more than 90 % for most HCV patients have become a reality and these results have been confirmed in real life experiences. The average treatment duration is 12 weeks. For some difficult-to-treat patients, 24 weeks seem necessary, while 8 weeks is sufficient for treatment naive, non-cirrhotic HCV genotype 1 patients with viral load < 6 MIO IU/ml with sofosbuvir (SOF) plus ledipasvir (LDV). Even shorter durations are presently being explored for future regimens. Preliminary results suggest that 6 weeks may become possible at least for easy to treat patients. While this seems to be the limit for chronic HCV patients, 4 weeks seem realistic for acute HCV.

HCV genotype 3 patients are now the most difficult to treat population. In particular for cirrhotic and treatment-experienced patients, an effective and safe 12 week regimen is still needed.

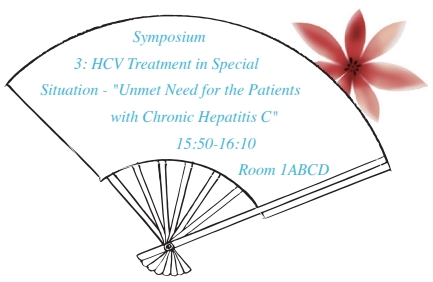
Preexistent NS5A mutants indicate a significant risk for treatment failure and they persist long term after treatment cessation. The relevance of viral resistance has to be studied further in DAA failure patients that are a very heterogeneous group. Neverthess, pretreatment routine testing for resistance-associated variants (RAV) seems to not be necessary for the average HCV patient.

With the advent of DAA therapies, prevention of recurrent HCV infection after liver transplantation has become possible. If patients achieve SVR before transplantation or are at least 30 days negative while under therapy, HCV recurrence is prevented. Eradication of HCV infection in the post-transplant population should be achieved soon in the years to come and a decline of transplantations for HCV induced liver disease should happen within the next decade.

SOF based DAA therapies have also been explored in decompensated liver disease, i.e. Child B and C cirrhosis. The majority of patients improve their MELD and CPT scores after achieving SVR. However, there are a proportion of patients that do not improve or even deteriorate. The definition of the point of no return is a major unmet need and still an unsolved problem.

Renal insufficiency is another yet unsolved problem in particular in the decompensated patient since SOF-based regiments cannot be given to patients with GFR< 30 ml/min. On the other hand, the so-called 3D combination (Paritasvir, Ombitasvir, Dasabuvir) can be given to patients with renal insufficiency but is either not recommended or contraindicated in decompensated liver disease. Novel regimens are needed for patients with decompensated liver disease and renal insufficiency. Whether SVR following successful DAA therapies protects from de novo infections at least in a proportion of patients also needs to be clarified.

But all the above issues might be a piece of cake when compared with the last but the most important unmet need: the global access to HCV therapies. A global strategy for HCV eradication is urgently needed.



Don't Miss Tomorrow

08:45 - 09:00	Room 1BC	Presidential Lecture
09:00 - 10:30	Room 1BC	Presidential Plenary
09:00 - 10:20	Room 1A	Session 1. HBV Treatment in Various Countries
09:00 - 10:20	Room 1D	Session 2. Significance of HBV Markers for Clinical Use
09:00 - 10:00	Room 2	Session 3. Recent Progress in ALF
10:45 - 11:05	Room 1BC	Lecture 1. Hepatitis B Treatment
11:05 - 11:25	Room 1BC	Lecture 2. Hepatitis B in EU
11:25 - 11:45	Room 1BC	Lecture 3. Serum HBsAg and AFP Levels during Acute Hepatitis Flare of Chronic Hepatitis B: A New Look in the Natural Course and Antiviral Therapy
10:45 - 11:45	Room 1D	Session 4. Treatment Towards HBsAg Clearance
13:30 - 15:30	Room 1D	Session 5. Basis for Hepatitis Treatment
13:30 - 14:50	Room 1BC	Symposium 6. Novel Therapeutic Strategies for HBV
14:50 - 17:25	Room 1BC	Symposium 7. Treatment of HBV for a Cure
13:30 - 15:25	Room 2	ACLF Working Party MTC
15:45 - 17:05	Room 1A	Symposium 8. Reactivation and Occult Infection of HBV
15:45 - 17:25	Room 1D	Session 6. Novel Approach for Viral Research

One Treatment for All Patient Populations with HCV Infection

Chronic hepatitis C virus (HCV) infection is the main cause of cirrhosis and hepatocellular carcinoma and it is estimated that more than 110 million people are chronically infected with HCV worldwide. Efficient antiviral treatment can reduce the risk of developing liver complications, however, poor efficacy and tolerability of current antiviral therapies have limited treatment uptake to <1%.

This afternoon, Professor Edward Gane from Auckland Clinical Studies Ltd., New Zealand will give a lecture entitled "HCV Therapy-One Treatment for all Populations".

With more than 100 direct acting antivirals (DAAs) having entered clinical development, the era of new DAAs has come. Recently, there were three combinations, ledipasvir/sofosbuvir, ombitasvir (ritonavir-boosted)/paritaprevir plus dasabuvir and elbasvir/grazoprevir, that completed Phase III development that could achieve sustained virological response (SVR) rates >95% in patients with HCV genotype (GT) 1 infection, including cirrhotics and treatment-experienced.

The oral pangenotypic regimen, sofosbuvir plus pangenotypic NS5A inhibitor velpatasvir for 12 weeks was confirmed to be highly efficient with an SVR of 95-100% in GT 1-6 HCV infected patients in the Phase III ASTRAL studies. Using the next gen NS5A inhibitor ABT-530 plus next gen PI ABT-493 for 8-12 weeks in the Phase II SURVEYOR studies, an SVR of 94-100% could be achieved in patients with HCV GT 1, 2 or 3 chronic infection.

Now, DAA triplets are being developed to shorten treatment duration and salvage DAA failure patients. In the small Phase II LEPTON study, sofosbuvir/velpatasvir plus the pangenotypic protease inhibitor GS-9857 for 8 weeks could achieve an SVR of 100% in HCV GT1 and GT 3 infected patients with cirrhosis. However, the SVR rates were lower in DAA failures, suggesting that the treatment duration should be prolonged for these patients. In another small Phase II C-CREST study, 8 weeks of grazoprevir plus NUC NS5B inhibitor MK-3682 plus the next gen NS5A inhibitor MK-8508 could achieve an SVR of 92% in patients with HCV GT 1, 2 or 3 infection.

These pangenotypic and ultrashort regimens represent the final phase of DAA development, with SVR rates above 95% across all patient populations. Combined with DAA access programs, public awareness and community-based targeted testing campaigns, global eradication of HCV should be feasible within the next 50 years.

Edward Gane

Symposium
3: HCV Treatment in Special Situation - "HCV Therapy-One Treatment for All Populations"
14:55 - 15:15
Room 1ABCD