

Hepatitis B and C Public Policy Association NEWSLETTER

MAY 2012 ISSUE

Dear Colleagues,

This newsletter conveys the message by Dr. Mark Thursz, EASL Secretary General, commenting on the successful outcome of the annual meeting of the Association held in Barcelona, along with an interview with the discoverer of HCV, Dr Michael Houghton, on the perspectives for a vaccine to prevent and treat this lethal infection. Prof. Jordi Bruix from Barcelona, the founder of modern hepato-oncology, shares a talk with us on the need for standardized guidelines and future research

lines for HCC, whereas Dr Kevin Fenton from CDC Atlanta, addresses the never ending issue of the cost-utility ratio of population screening for HCV counterbalanced by the thoughts of Charles Gore, Chief Executive of the patients advocacy Hepatitis C Trust.

Massimo Colombo, Editor

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Update on Activities

Overview of policies for prevention, care and treatment of hepatitis B and C

Prof. Angelos Hatzakis and Prof. Harry Janssen have produced an extensive slide deck based on the material which was presented, some of it for the first time, at the conference on Hepatitis B and C in Europe which the Association held in October 2010 in Brussels under the auspices of the Belgian EU Presidency.

The slide deck – 'An Overview of Policies for the Prevention, Care and Treatment of Hepatitis B and C' – is intended as a public tool, for education and as a basis of discussion with stakeholders including national authorities.

It is freely available for downloading on the Association's website www.hepbcppa.org.

Summit Conference on hepatitis B and C in Mediterranean and Balkan Countries

The Association will hold this Conference in December 2012 in Cyprus under the auspices of the forthcoming Cyprus EU Presidency, to present new and existing data and permit targeted discussion with the objective of promoting common strategies on the prevention and management of these diseases. The Conference will support the broad programme of the European Commission and the European Centre for Disease Prevention and Control (ECDC), as well as the Resolution on Viral Hepatitis adopted at the 63rd World Health Assembly in May 2010.

Further information on the Conference will become available on its website www.hepsummit2012.org which will go live shortly.



EASL's Activities

Mark Thursz, EASL Secretary-General

This has been quite a busy time of the year for the EASL office team and for the EASL Secretary General as we prepared the International Liver Congress which was held in Barcelona.

The programme is developed at least a year in advance, in fact the EASL Governing Board met last week to put together the framework for the 2013 Congress, and it is

always a challenge to ensure that there is plenty of interesting sessions for all of the conference attendees. Over recent years we have tried to maintain some key themes throughout the congress so that specialists will find something to their taste at all (or most) times. Viral hepatitis appears as a dominant theme. This clearly irritates some people but I feel that it can easily be justified. At one level this is one of the most exciting eras ever in the development of

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new treatments for hepatitis C. No I underestimate, this IS the most exciting era; in my view not just an evolution of therapy but a revolution with the realisation of interferon-free regimens. In parallel with these developments there is still a strong thread of basic virological research on viral replication and immune responses to viral infection. Viral hepatitis is now one of the aetiologies of liver disease that is most susceptible to medical intervention. Other themes which run through the congress include liver cancer, basic science, alcoholic liver disease (the topic for this year's post-graduate course) and, for the first time this year, paediatric liver disease.

One theme that has enjoyed growing popularity over the last few years is public health and epidemiology. I perceive that more of the EASL community have come to appreciate the importance of public health in the field of liver disease and understand the need to interact with epidemiologists and public health

professionals. No doubt some are motivated by the need to justify grant applications or manuscripts on the basis of disease burden statistics whilst others need data to justify clinical resources. All of us need to understand the burden of morbidity and mortality attributable to liver disease and the approaches required to reduce the impact of these diseases. This year two sessions focused on epidemiology and public health; one on the burden of disease and the other on the impact of EU policy. These sessions delivered stimulating lectures and led to a constructive debate. These are areas of overwhelming importance to EASL as they are central to our lobbying activities in the European Governmental institutions. Working with the Hepatitis B & C Public Policy Association, the European Liver Patients Association and the World Hepatitis Alliance, EASL has been advocating for screening and surveillance for hepatitis B & C throughout Europe. Whilst

it seems obvious to those of us who work in Hepatology it remains incomprehensibly obscure to the politicians and civil servants in Brussels and member state governments that screening is required to identify cases of an asymptomatic infection in order to reduce the burden of end-stage liver disease.

Burden of disease is a strong political motivator and concern has been expressed within the EASL Governing Board that there is insufficient data in the public domain on liver disease in Europe. As a starting point we have commissioned a systematic review of published data. We are grateful to Francoise Roudot-Thoraval and her group for completing this task so swiftly. To my mind this report, which will be published later this year, vindicates our professional concerns about the number of patients we are seeing in clinics.

The role of patients' associations in Europe

Charles Gore, Chief Executive of the Hepatitis C Trust

Q: Charles, it seems to us that there has been a recent increase in awareness toward viral hepatitis probably as the consequence of the WHO resolution. Do you agree, or do you think we still have a long way to go?

I think there is definitely an increased level of awareness amongst governments. The Alliance is constantly in correspondence with individual Ministries of Health and uses the annual WHO World Health Assemblies as opportunities to engage with all countries and so we will, for example, be addressing all 194 Member States at this year's Assembly in May to press for further action.

I think, however, there is indeed still a long way to go to increase awareness amongst the general population or amongst at-risk

groups. As you know, World Hepatitis Day is now one of only four official WHO disease-specific awareness days, the others being for AIDS, TB and malaria (World cancer Day, for example, is not an official day). Last year was the first one and, despite the fact that all Member States 'resolved' to mark it, very few in fact did, although community groups took part in over 80 countries. We have changed our way of working with WHO in the organization of the Day so we expect many more governments to participate this year. In addition, World Hepatitis Day is a specific part of the new WHO global viral hepatitis strategy and the Alliance is in the process of agreeing a monitoring role on behalf of WHO so that there will be an annual public record of each country's awareness-raising efforts.

Q: Which are the top priorities of your association for the next years?

Now that WHO has developed the global strategy, which we worked very hard to ensure was part of the 2010 resolution, the Alliance's goals are to ensure that every WHO region has a regional strategy and every country has a national strategy, all based on the four axes of the global strategy, which are: Partnership, mobilization and communication; Data for policy and action; Prevention of transmission; and Screening, care and treatment. Once strategies are in place we will be working to ensure they are funded and implemented.

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One of the key ways of doing this will be to strengthen the patient voice and our goal here is to create one that is as powerful as that in HIV/AIDS, however ambitious that sounds. Currently we work with 300 patient advocacy groups in 60 countries, of which 140 are full members of the Alliance but we are aiming to have at least one group in every country where viral hepatitis is an issue, which is of course the great majority of countries; we will also be working to ensure that patient advocacy groups are sufficiently skilled in advocacy, media relations and fundraising to keep a sustainable, constant pressure on governments. The Alliance will be supporting this by annually monitoring each government's hepatitis prevention and control work.

Q: Patients with Hepatitis C are going to benefit from the introduction of the first two directly acting antivirals that will increase cure rates in most. However, these drugs will also increase health care costs and might be precluded to some patients by local health authorities. Do you think patients

advocacies should play a role in shaping the eligibility rules? And how so?

This is a difficult question. I personally believe that patient advocates should advocate for what the patients in their country want and should consult those patients to discover what that is. This might mean arguing that the new drugs should be available to all who want them, as I did in the UK in my other capacity as CEO of The Hepatitis C Trust; happily the relevant authorities, the Scottish Medicines Consortium and NICE, agreed. I believe it is up to the budget holders to argue for restrictions, not for us.

The issue is that there is no logical reason to consider prioritisation only from the view of perceived medical 'need'. Are you going to exclude the woman who wants to have a child but is not prepared to take the risk of maternal transmission and is approaching the end of her fertile years, just because she has no liver damage? What weight will you give to a doctor who wants to qualify as a surgeon whose work will involve exposure prone procedures? Are

you going to ignore people who 'might' not adhere to the difficult treatment regimen quite as well, such as drug users and people going through highly emotional divorces? Must they all try a clearly inferior treatment first, no matter that it is very hard? And if they don't want to? Must they wait? For what? Till when?

I believe that patient advocacy groups must fight for the totality of people living with viral hepatitis, not just for certain groups. This has always been the policy of the World Hepatitis Alliance. We represent people with hepatitis B and with hepatitis C, drug users and those co-infected with HIV, people in the developed world and in the least developed countries, those infected today and those at risk of becoming so in future years, those with common genotypes and those with the rarer ones. We represent them all and we do not favour one group at the expense of another. Governments have always used 'divide and rule' to force through their will. As patient advocacy groups we must be united and speak with a single voice. Then we cannot be ignored.

HCC a hot topic in Europe: epidemiology, guidelines and future research lines

Professor Jordi Bruix, Chief of Barcelona Clinic Liver Cancer (BCLC) Group, of the Liver Unit, Hospital Clínic, University of Barcelona

Q: Prof Bruix, could you briefly summarize the current epidemiological data on hepatocellular carcinoma incidence in Europe

The epidemiology of HCC in Europe is

heterogeneous due to the different prevalence of risk factors in the population. In Southern Europe the prevalence of HCV infection has decreased as the major spread occurred earlier as compared to Northern Europe. There, alcoholic liver disease keeps being a relevant etiologic factor

but cases related to HCV and non-alcoholic steatohepatitis are on the rise. In general, the incidence of HCC is not increasing globally and the age at diagnosis has increased reflecting the age profile of patients infected with HCV. Interestingly, while the incidence of HCC

is stable of slightly decreasing, there is a slight increase in the incidence of intrahepatic cholangiocarcinoma. This cancer also emerges in cirrhotic livers and the mechanisms for its development is largely unknown.

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Q: When discussing hepatocellular carcinoma is Europe different than other geographical areas such as the USA or Asia? And if so do you think is there a need for "regional" strategies/guidelines or does one fit all?

The distribution of risk factors and the profile of patients may differ. In the USA nonalcoholic steatohepatitis linked to obesity is a major issue while this is not the case in Europe.

Nevertheless, the strategies for diagnosis and treatment should not be different according to regions. Indeed, practice guidelines in Europe and USA developed by several scientific associations such as EASL, ESMO, AASLD or WGO, do not show major differences. Of course, profiling of patients will differ in patients with HCV as compared to patients with obesity, and tailoring of clinical decision making according to specific profile should sure be in place as in any other condition.

Q: If one had to choose, do you think future efforts should concentrate more on prevention of HCC or on developing better therapies, given that survival after diagnosis is still subpar these days?

It is clear to me that major efforts and priority research should be devoted to prevention of HCC rather than in intervention at advanced stage. The impact in the community will be more valuable in the first

approach, but this should not be seen as the other area to be neglected. Detection of HCC at an early stage with understanding of the molecular mechanisms leading to overt malignant profile should also be a major goal. This will prime a reduction of cancer related death and development of targeted therapies to prevent transition into advanced stages.

Some thoughts on the development and need of a vaccine against HCV

Michael Houghton, the discoverer of the hepatitis C virus and Professor of Virology, at the Department of Medical Microbiology and Immunology of the University of Alberta in Canada

Q: Dr Houghton, it has been some years since your group discovered the Hepatitis C virus, in these years much has been learnt and many drugs are in development, but the development of a vaccine is still somewhat of a mirage. Is this true?

Well, progress has been slow due to the lack of a convenient animal model and the inability until recently, of being able to assay for neutralizing antibodies. However, Okairos have a promising vaccine candidate in phase 2 human efficacy testing now for HCV. It is based on adenoviruses expressing the HCV nonstructural proteins in order to elicit broad, cross-protective cellular immune responses. The phase 1 immunogenicity data look promising as does the pre-clinical efficacy data in animals but it is hard to predict just how effective it will be in humans. We will know in 2-3 years time at the conclusion of their phase 2 trial.

In addition, we have learnt recently that envelope glycoprotein-based vaccines derived from a single strain of HCV can elicit broadly cross-neutralising antibodies in mice, guinea pigs, macaques and chimpanzees. Very recent data from my lab here at the University of Alberta has shown that some phase 1 human trial volunteers respond to such a vaccine by

making antibodies that can inhibit the infectivity in vitro of all the major global strains of HCV meaning that we could possibly protect against the vast heterogeneity of HCV with such a vaccine, but of course, efficacy data in humans is needed in the future to confirm this.

In conclusion, I believe that a HCV vaccine is definitely feasible and that we will see one available within the next decade, approximately.

Q: There seem to be many promising drugs for HCV infection that could actually achieve cure rates close to 100%, do you think there is still place for the development of a vaccine?

Definitely yes. The great progress in HCV drug development will take several decades before it starts to influence global transmission rates. With many hundreds of thousands of new HCV infections occurring around the world every year, there is still an urgent need for a prophylactic vaccine that is cheap and well-tolerated in comparison with the very expensive drug cocktails under development which are also accompanied with significant adverse effects during the many weeks of therapy.

Quick Q & A session on HCV screening with Dr. Kevin Fenton

Dr Kevin Fenton, Director of the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention at the Center for Disease Control and Prevention in Atlanta, Georgia USA.

Q: Dr. Fenton could you briefly explain to us what is a screening program for a disease?

The World Health Organization (WHO) defines screening as the presumptive identification of unrecognized disease or defect by application of tests, examinations, or other procedures which can be rapidly applied. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment.

Q: What about HCV infection? What are the current screening recommendations, and do they actually work?

Current CDC guidelines for HCV screening were issued in 1998 and rely on a risk-based approach to screening. These risk factors include individuals with a history of injecting drugs, a blood transfusion before 1992, and chronic hemodialysis patients.

With up to 80% of people chronically infected with HCV still unaware of their status, that approach clearly is not sufficient. Not enough people are getting tested and diagnosed. Many people with chronic HCV infection either don't remember risks from many years ago, or are unwilling to admit risks. And clinicians frequently don't ask patients, or don't test even when they are aware of risks.

Q: Do you have any suggestions to modify and improve the current strategies?

CDC hosted a meeting in 2011 of invited expert consultants (hepatitis clinicians, research scientists, public health practitioners, and advocates) to assist CDC with an evaluation of the evidence base that will be used to issue updated guidelines for HCV testing and referral to care. CDC is developing these updated guidelines to help improve identification of people with HCV infection who are in need of care.

