2017
World Indigenous Peoples’ Conference on Viral Hepatitis

The International Coalition to Eliminate Hepatitis B.
HBV is currently incurable...

• However functional cure (HBsAg seroclearance) is observed in a small number of patients, either spontaneously or in the setting of antiviral therapy.

• This is encouraging and suggests functional cure (at the very least) is a realistic goal.
2016 : Establishment of an international coalition dedicated to the elimination of HBV

- ICE-HBV (International Coalition to Eliminate HBV)
  - Representatives from Academia (basic and clinical sciences) and the HBV affected community.
  - Facilitate the establishment of subgroups for Virology, Immunology, Innovative Tools, Clinical Studies.
  - Four pillars of HBV research to drive and coordinate HBV cure programs worldwide
AIM

To support the discovery of a safe, affordable, scalable and effective cure, available to all persons living with CHB. To achieve this, our vision is to create an international, independent, research-based and patient-centred forum in order to coordinate, promote and foster collaborative partnerships working towards a cure for HBV.
Inspired by “Towards an HIV Cure”

- HIV Cure initiative established to facilitate scientific discussion, exchange and collaboration to promote and accelerate research towards a HIV cure

- Multidisciplinary International Working Group works in consultation with industry, patients and advocacy groups, research funders and regulatory agencies:
  - Subgroups on virology, immunology, innovative tools, cost-utility, ethics and social sciences.
  - HIV Cure Advisory Board
  - HIV Cure Industry Liaison Group

- Results: Two HIV Cure Strategies, Increased Research Funding, Important Findings and Learnings from Failures (Visconti, reactivation, biomarkers). Numerous International Collaborations
We published a “Call to Arms”

PERCEPTIONS

Global strategies are required to cure and eliminate HBV infection

Peter Revi, Barbara Testoni, Stephen Locarnini and Fabien Zoulim

Abstract Chronic HBV infection results in >1 million deaths per year from cirrhosis and liver cancer. No known cure for chronic HBV exists, due in part to the continued presence of transcriptionally active DNA in the nucleus that is not directly targeted by current antiviral therapies. A coordinated approach is urgently needed to advance an HBV cure worldwide, such as those established in the HBV field. We propose the establishment of an International Coalition to Eliminate Hepatitis B Virus (ICE-HBV) to facilitate the formation of international working groups on HBV virology, immunology, innovative tools and clinical trials to promote awareness and education as well as to drive changes in government policy and ensure funds are channelled to HBV cure research and drug development. With the ICE-HBV in place, it should be possible to enable an HBV cure within the next decade.

Over 240 million people worldwide are chronically infected with HBV and, although a prophylactic vaccine and effective antiviral therapies are available, no cure exists. Curative regimens are urgently needed because up to one million deaths per year are caused by HBV-related liver cancer and end-stage liver disease. We believe it is imperative that research to develop an HBV cure is coordinated on a global scale. Building on momentum established at the HBV Cure Workshops in Paris in 2014 and 2015 organized by ANRS (Agence Nationale pour la Recherche contre le SIDA et les Harrétiques), the International Workshop on Antiviral Drug Resistance: Meeting the Global Challenge in Berlin in 2014, and HBV cure workshop at the 13th International Symposium on Viral Hepatitis and Liver Disease in Berlin in 2015, this paper calls for the establishment of an International Coalition to Eliminate the Hepatitis B Virus (ICE-HBV), to work together to develop strategies for a cure.

Establishment of the ICE-HBV
The ICE-HBV would consist of working groups made up of leaders in the HBV field, both basic researchers and clinicians across continents, similar to groups established through the International AIDS Society, which has established the HIV care advisory board and a multidisciplinary international working group of researchers dedicated to developing an HIV cure. The working group consists of subgroups for Virology, Immunology, Innovative Tools and Clinical Trials. The aim of the ICE-HBV initiative is to: first, to facilitate scientific discussion, exchange and collaboration to promote and accelerate research towards a cure for HBV; second, to provide leadership in advocating for increased investment and resource optimization in HBV cure research; and third, to provide and disseminate clear and accurate information to the broader community. These aims are facilitated through consultation with industry (pharmaceutical and biotechnology), patients and advocacy groups, research funding bodies and regulatory agencies. This initiative has seen the establishment of dedicated HBV care symposiums held each year since 2010, in Vienna, Washington D.C., Kuala Lumpur, Melbourne and Vancouver, respectively. We believe similar approaches can be adopted for HBV ICE-HBV would function as the multidisciplinary international working group with representatives from academia, industry and the HBV-affected community, which would facilitate the formation of subgroups in each of the four major disciplines namely, Virology, Immunology, Innovative Tools and Clinical Trials etc. Ensuring that each of these working subgroups include representatives from Asia-Pacific, Africa and South America, where much of the HBV burden lies, is imperative.

Current HBV treatments and cure
Current antiviral therapy for chronic HBV infection is limited to immunomodulatory treatments such as interferon, or to direct-acting antiviral agents (DAAs), the most efficacious of which are emtricitabine and tenofovir. Interferon upregulates a range of antiviral interferon-stimulated genes (ISGs) to modify the covalently closed circular DNA (cccDNA) epigenome, control viral replication and stimulate natural killer (NK) cell activity, whereas DAAs act directly on viral replication by inhibiting the reverse transcription of pregenomic RNA to DNA. These treatments are not curative, as they do not directly target cccDNA, although in the past few years it was shown that interferon treatment might diminish cccDNA transcriptional activity and also lead to partial loss of cccDNA, at least in some cell culture systems. For reasons that are unclear, the efficacy of interferon therapy is dependent on HBV genotype, working best for genotypes A and B, and less well in genotypes C and D. Given that treatment response still remains far from satisfactory in the majority of treated patients, some studies have reported long-term benefits of interferon treatment, with a meta-analysis of 12 studies showing that the risk of progression to hepatocellular carcinoma (HCC) reduced by 34%, with greatest benefit in patients with cirrhosis. Studies have shown that continued DAA treatment might lead to hepatitis B surface antigen (HBsAg) seroclearance in ~10% of patients after >5 years of administration, but the underlying mechanism remains unclear. Other meta-analysis showed that the risk of HCC after DAA treatment was reduced by 38%, with greatest benefits observed in patients without cirrhosis. Although the long-term benefits of first-generation DAAs (lamivudine and adefovir) have been manifested in reduced progression...
Provisional Governing Board

• Chair Peter Revill
• Co-Chair Fabien Zoulim
• Members
  • Massimo Levrero
  • Stephen Locarnini
  • Jake Liang
  • John Tavis

Discussions are underway regarding expanding the membership of the board to include representatives from Asia and Africa, as well as key organisations and patient forums.
“Thanks to recent technological breakthroughs, the HBV scientific community finally has a chance to discover a durable cure for chronic HBV infection. Everyone involved in the ICE-HBV initiative is fully committed to achieving that goal. I look forward to doing everything I can to encourage global cooperative research focused on eradication and/or permanent silencing of the viral cccDNA transcriptional template and development of innovative immunological approaches that prevent viral spread and selectively eliminate HBV-infected cells”.

www.ICE-HBV.org
SubGroups for Virology, Immunology and Innovative Tools

- Virology: Chairs Maura Dandri and Haitao Guo
- Immunology: Chairs Adam Ghering and Robert Thimme
- Innovative Tools: Chairs Jianming Hi and Fengmin Lu

Working together since February 2017

- Clinical Studies Co-Chairs selected in March 2017: Seng Gee Lim, Harry Janssen, Pietro Lampertico
Stakeholders Consulting Group

• Chairs: Ulla Protzer (DZIF), Tim Block (The Hepatitis B Foundation), Veronica Miller (HBV Forum).

• This group will provide critical feedback and advice to the Governing Board and working groups:

  • Who should be in ICE-HBV?
  • Which activities should be undertaken?
  • Coordination of initiatives
What are the working groups doing?

• Produce a joint position paper on what will be needed to achieve HBV cure, similar to papers published in the HIV field (Deeks et al. Nat. Med. 2016).

• Support specific projects on HBV cure research
  • cccDNA assay standardization

• Promote HBV cure initiatives to increase funding for HBV research world wide.
Industry

• We are defining our engagement strategy and rules

• Working with the HBV Forum on regulatory questions

Senior Strategic Advisors

• First appointee - Professor Raymond Schinazi
Strategy Development

- GB, Working Groups and Stakeholders met at EASL in Amsterdam in April => brainstorming phase.
- Working groups to meet at the International HBV meeting in Washington in September => prioritization phase.
- Consultations with researchers and other stakeholders worldwide in September - February 2018
- Revision in February-April 2018
- Strategy Publication in September 2018

In addition, ongoing creation of project teams for specific research purposes, such as the cccDNA assay team
Promotion

• Partners with the ANRS HIV Cure Workshop in May, the Science of HBV Cure in Singapore and the International HBV Meeting

• Australian launch at the Doherty Institute on World Hepatitis Day (28 July, Webinar available)

• World Hepatitis Day Campaign participation

• World Hepatitis Summit Nov 2017

• WIPC for Viral Hepatitis, August 2017.

• Hep DART 2017 in Hawaii

• EASL 2018 in Paris

• Global Hepatitis Summit Toronto June 2018

• ICE-HBV @ any more regional & local meetings, plus one on one coalition building meetings.
Join us to cure chronic hepatitis B!!
Acknowledgements

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Peter Revill
Fabien Zoulim
Massimo Levrero
Jake Liang
John Tavis

ICE-HBV Groups
Scientific Working Groups
Stakeholders Group

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