
HBV Forum 4: Evaluation Report

April 12, 2018

Novotel Paris Pont Sevres Hotel

Paris, France

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HBV FORUM SPONSORS



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HBV FORUM STEERING COMMITTEE MEMBERS

CATEGORY	NAME	AFFILIATION
Academic	Carol Brosgart, MD	University of California San Francisco
Academic	Henry LY Chan, MD	The Chinese University of Hong Kong
Academic	Jordan Feld, MD, MPH, FRCP	Toronto Western Hospital Liver Center
Academic	Seng Gee Lim, MD	National University of Singapore
Academic	Robert Gish, MD	Stanford Robert Gish Consultants LLC
Academic	Marion Peters, MD	University of California San Francisco
Academic	Fabien Zoulim, MD, PhD	INSERM – French National Institute of Health
AASLD	Anna Lok, MD	American Association for the Study of Liver Diseases (AASLD) University of Michigan
EASL	Prof. Markus Cornberg	European Association for the Study of the Liver
HBV Foundation	Timothy Block, PhD	Hepatitis B Foundation
ICE-HBV	Peter Reville, PhD	International Coalition for the Elimination of HBV (ICE-HBV) University of Melbourne
Community	Joan Block, RN, BSN	Hepatitis B Foundation
Community	Michael Ninburg, MPA	Hepatitis Education Project
Forum	Veronica Miller	Forum for Collaborative Research
Industry	Gavin Cloherty, PhD	Abbot Diagnostics
Industry	Anuj Gaggar, MD, PhD	Gilead Sciences Inc.
Industry	Bruce Givens, MD	Arrowhead Research
Industry	Oliver Lenz, PhD	Janssen Pharmaceuticals ID&D
Industry	Ed Marins, MD	Roche Molecular Systems
Industry	William (Bill) Symonds, PharmD	Arbutus Biopharma
Regulatory	Filip Josephson, MD, PhD	Swedish Medical Products Agency
Regulatory	Poonam Mishra, MD, MPH	US-Food and Drug Administration

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HBV FORUM 4 - MEETING AGENDA

5:30 PM	Light Refreshments & Registration	
6:30 PM	Welcoming Remarks	Veronica Miller, William (Bill) Symonds Pedro Goicochea
6:40 PM	Effects on Combination Therapy on Achieving Cure	Barbara Testoni
6:55 PM	Modelling Kinetics of HBV DNA and Recommendations for Moving Forward	Alan Perelson
7:10 PM	Expanding Immune Monitoring in HBV Trials - Part I	Adam Gehring
7:20 PM	Expanding Immune Monitoring in HBV Trials - Part II	Mala Maini
7:30 PM	Roadmap on HBV at EASL 2018	Robert Gish
7:40 PM	Break	
8:00 PM	General Discussion	Veronica Miller, William (Bill) Symonds
8:10 PM	HBV Cure Roadmap: Follow-up from Hepatitis B Foundation Meetings with NIAID, NIDDK and NCI Regarding an NIH HBV Cure Agenda	Carol Brosgart
8:20 PM	HBV Cure Initiatives in the AIDS Clinical Trials Group (ACTG)	Mark Sulkowski
8:40 PM	Community Perspectives on the Road to HBV Cure	Joan Block Maureen Kamischke Michael Ninburg Su Wang
9:00 PM	Adjourn	
9:00 PM	Networking Reception	

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BACKGROUND

Launched in January of 2016, the HBV Novel Therapeutic Interventions (The HBV Forum) aims at advancing the regulatory science for HBV and its associated morbidities by providing an independent and neutral environment for ongoing multi-stakeholder dialogue.

The HBV Forum is currently comprised of 195 members representing different stakeholder groups, including members of academia, researchers, representatives of pharmaceutical and diagnostic companies, regulators from the US and Europe, and patient advocates/representatives.

The HBV Forum has a Steering Committee (SC) consisting of 22 members that provide overall scientific leadership, suggest topics for consideration, and prioritize the research questions to be addressed in the project.

The HBV Forum currently has two working groups and two sub working groups:

- **Surrogate Endpoints Working Group**

Co-chairs: Marion Peters, MD and Oliver Lenz, PhD.

Aim: Strengthen the link of surrogate markers (endpoint in clinical studies) with long term clinical outcomes (e.g., liver disease progression/HCC)

- **Diagnostics/Biomarkers Working Group**

Co-chairs: Ed Marins, MD and Gavin Cloherty, PhD.

Aim: Develop clarity on what is needed for biomarker acceptance and validation for HBV drug/diagnostic development

- **Treatment Combination Working Group**

Co-chairs: Prof. Lim Seng Gee, MD and Bruce Given, MD.

Aims: I.) Provide clarity on the requirements of novel agents in clinical development, and II.) identify mechanisms to speed up the development of combinations of different promising agents across companies

- **Liver Safety Monitoring sub Working Group.**

Co-chairs: Robert Fontana, MD and Maria Beumont-Mauviel, MD

Aim: to facilitate HBV drug development by developing consensus terminology and definitions for industry, regulators, and investigators to use when testing the safety and

efficacy of novel therapeutic agents for chronic HBV when used alone or in combination with other investigational or approved anti-HBV agents.

Since its creation, the HBV Forum has held four forums:

- HBV Forum 1: Boston, Massachusetts; November 15th, 2016
- HBV Forum 2: Amsterdam, the Netherlands; April 18th, 2017
- HBV Forum 3: Washington, District of Columbia; October 24th, 2017
- HBV Forum 4: Paris, France; April 12th, 2018

This document presents the evaluation of HBV Forum 4.

HBV FORUM 4

HBV Forum 4 took place on April 12, 2018, from 6:00 – 9:00 pm at the Novotel Paris Pont Sevres Hotel, in Paris, France following the International Liver Congress 2018 organized by EASL.

One hundred eleven (111) HBV Forum members registered to attend HBV Forum 4; however, only 103 people participated in the meeting; 84 in person and 19 remotely.

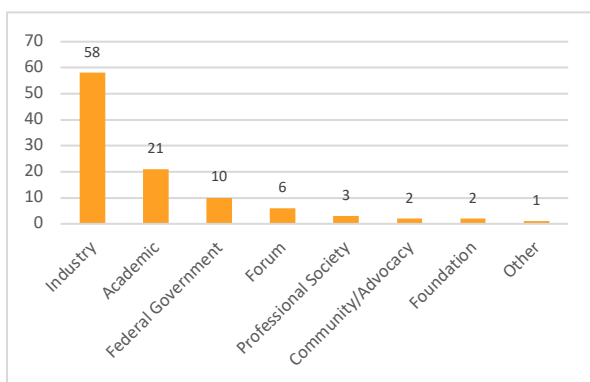


Figure 1: Distribution of registered participants by type of organization
[Other: Mayo Clinic]

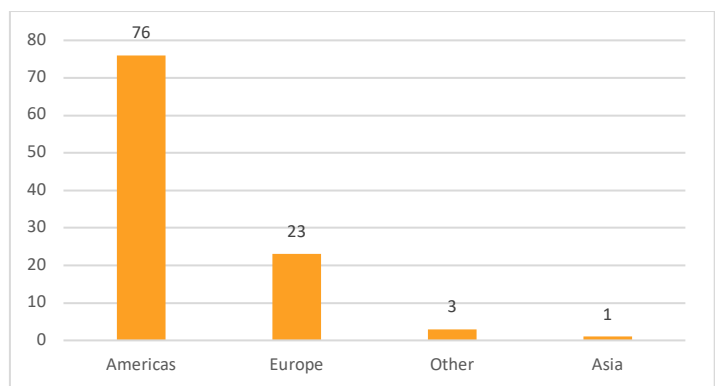
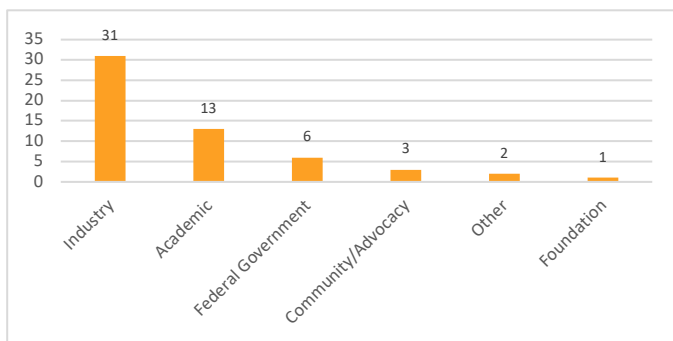


Figure 2: Distribution of registered participants by continent
[Other: New Zealand & Australia]

HBV Forum 4 Evaluation

The HBV Forum 4 Evaluation was distributed to people that registered to the meeting on April 16th, 2018 using SurveyMonkey ©. Responses were collected through May 15th, 2018, and reminders were sent on a weekly basis until the data collection phase was closed.

A total of 58/111 survey recipients (52%) responded to the 35 questions evaluation. For 13 of the respondents (22%) HBV Forum 4 was the first time attending any HBV Forum.



More than half of HBV Forum members that responded the evaluation survey (53%) were representatives from industry, followed by representatives from academia (22%) and 10% of representatives from the Federal Government. (See Figure 3)

Figure 3: *Distribution of evaluation respondents by type of organization*

Of the participants that represented the industry, 21/31 (68%) reported working for a pharmaceutical company, and 7/31 (23%) reported working for a diagnostics company. The remaining two industry representatives reported working for a contract research organization or CRO. Of these participants, 25% reported being directors of project leads, clinical researchers (26%) or chief medical officer or scientific officers (19%). The remaining seven reported performing other activities such as marketing, finances or venture capitalists.

In general, respondents perceived that HBV Forum 4 facilitated a platform for networking and facilitated and/or extended interactions among participants and new collaboration with individuals and organizations. Presentations and panels in HBV Forum 4 were perceived as valuable to participants' work and would help as guidance for future work in their organizations.

A few survey respondents (12%) considered that it was challenging to ask questions and/or to actively engage in the meeting discussions.

Participants responding to this evaluation survey will strongly recommend other professionals and industry representatives to join the HBV Forum and that would be interested to attend HBV Forum 5 in

San Francisco, California in November of 2018. Figure 4 presents a summary of the opinions with regards to this aspect of the meeting.



Figure 4: Overall opinions about HBV Forum 4

HBV FORUM 4 SESSIONS

HBV Forum 4 was originally organized in 13 sessions running from 6:00 pm to 9:00 pm, however, due to weather conditions, venue of the meeting and timing conflicting with a session at EASL, the meeting started 30 minutes later covering only 10 sessions. Presentations of the different sessions are available on the HBV Forum web page (<http://forumresearch.org/projects/hbv-forum/hbv-forum-meetings>).

The following sections describe the perception and opinions participants had with regards to the different sessions of HBV Forum 4.

SESSION 1: Welcoming Remarks

This 15 minutes session was moderated by Veronica Miller, Forum for Collaborative Research Executive Director and William (Bill) Symonds, HBV Forum co-chair, with a brief presentation by Pedro Goicochea, HBV Forum Program Manager, on the developments and achievements of the HBV Forum.

Respondents considered that the information presented during this session was important and valuable for purposes of the conduct of the HBV Forum (73% and 70.91% respectively) and that the session was adequate in length (94%).

SESSION 2: Effects of Combination Therapy on Achieving Cure

This session was a shared presentation between Fabien Zoulim and Barbara Testoni from *Institut National de la Santé et de la Recherche Médicale* (INSERM), but, the latter gave the presentation in full.

The session was reported to be appropriate in length (90%) and almost half of the respondents (45%) considered that it was a valuable component of HBV Forum 4. A little more than a third of the respondents strongly agreed that the information presented in the session helped to increase their understanding of the effect of combination therapy on achieving HBV cure and that were strongly planning to apply the new knowledge to their work or professional practice.

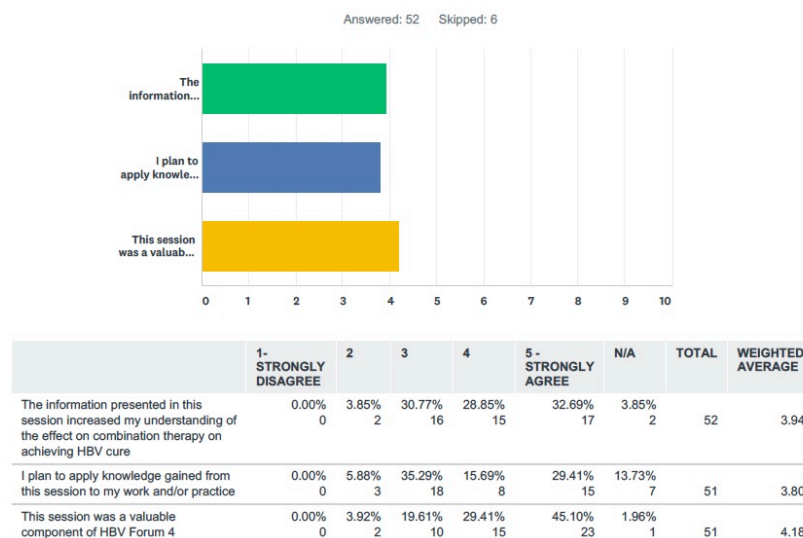


Figure 5: Opinions on Session 2

SESSION 3: Modelling Kinetics of HBV DNA and Recommendations for Moving Forward

Professor Adam Perelson from Los Alamos National Laboratory in the US, presented this session which was considered appropriate in length by 71% of respondents, however, almost a fifth (19%) indicated that the session was too long.

Opinions on this session are more dispersed, but an important proportion of respondents agreed and strongly agreed that the information presented helped to increase knowledge on modelling kinetics of HBV DNA and that the topic was a valuable component of HBV Forum 4.

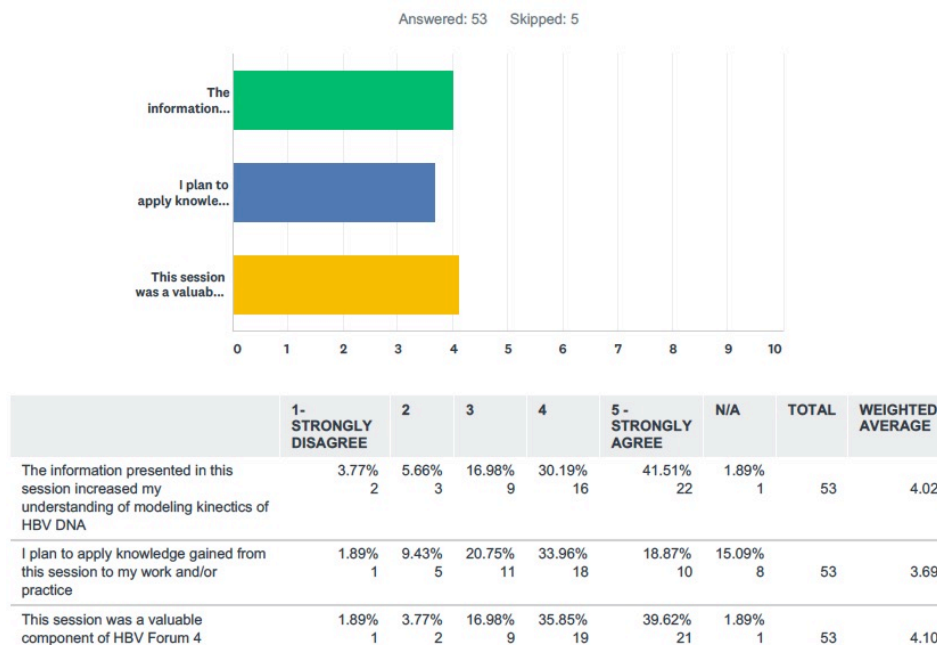
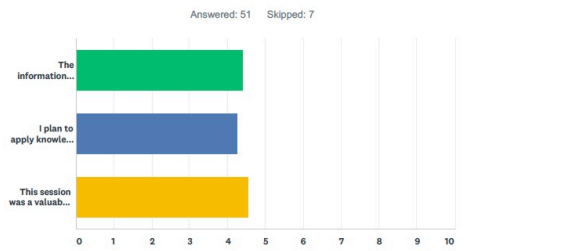


Figure 6: Opinions on Session 3

SESSION 4 – 5: Expanding Immune Monitoring in HBV Trials (Part 1 and 2)

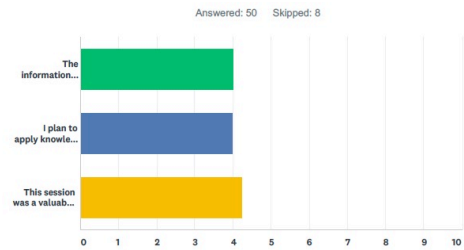
This session was comprised of two parts, the first one presented by Dr. Adam Gehring from the Toronto Center for Liver Disease/University of Toronto, and the second one presented by Dr. Mala Maini from University College London.

Both sessions were reported as appropriate in length and the contents were agreed and strongly agreed to be informational, applicable to respondents' professional practice and valuable component of HBV Forum 4. See Figures 7 and 8.



	1- STRONGLY DISAGREE	2	3	4	5 - STRONGLY AGREE	N/A	TOTAL	WEIGHTED AVERAGE
The information presented in this session increased my understanding of immune monitoring in HBV trials	0.00% 0	0.00% 0	11.76% 6	35.29% 18	50.98% 26	1.96% 1	51	4.40
I plan to apply knowledge gained from this session to my work and/or practice	0.00% 0	3.92% 2	9.80% 5	35.29% 18	39.22% 20	11.76% 6	51	4.24
This session was a valuable component of HBV Forum 4	0.00% 0	0.00% 0	7.84% 4	29.41% 15	60.78% 31	1.96% 1	51	4.54

Figure 7: Opinions on Session 4



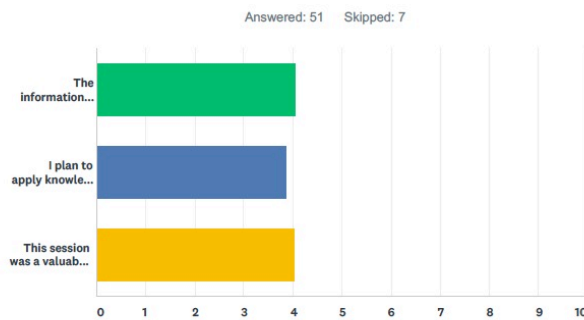
	1- STRONGLY DISAGREE	2	3	4	5 - STRONGLY AGREE	N/A	TOTAL	WEIGHTED AVERAGE
The information presented in this session increased my understanding of immune monitoring in HBV trials	0.00% 0	2.00% 1	30.00% 15	30.00% 15	36.00% 18	2.00% 1	50	4.02
I plan to apply knowledge gained from this session to my work and/or practice	0.00% 0	2.00% 1	24.00% 12	34.00% 17	28.00% 14	12.00% 6	50	4.00
This session was a valuable component of HBV Forum 4	0.00% 0	0.00% 0	20.00% 10	36.00% 18	42.00% 21	2.00% 1	50	4.22

Figure 8: Opinions on Session 5

SESSION 6: Roadmap on HBV at EASL 2018

This session was led by Robert Gish, HBV Forum steering committee member and consultant. He was requested to present on the different sessions, presentations and abstracts on HBV submitted and accepted at EASL’s International Liver Congress 2018. The session was considered as appropriate in length by two thirds of the respondents (78%), although 12% thought that it was too short.

The information provided in Dr. Gish’s session was agreed and strongly agreed to be helpful, useful and a valuable component of HBV Forum 4.



	1- STRONGLY DISAGREE	2	3	4	5 - STRONGLY AGREE	N/A	TOTAL	WEIGHTED AVERAGE
The information presented in this session helped me identify the different discussions taking place at the International Liver Congress 2018	0.00% 0	3.92% 2	21.57% 11	33.33% 17	35.29% 18	5.88% 3	51	4.06
I plan to apply knowledge gained from this session to my work and/or practice	1.96% 1	1.96% 1	31.37% 16	21.57% 11	29.41% 15	13.73% 7	51	3.86
This session was a valuable component of HBV Forum 4	1.96% 1	1.96% 1	23.53% 12	29.41% 15	37.25% 19	5.88% 3	51	4.04

Figure 9: Opinion of Session 6

SESSION 7: HBV Cure Roadmap: Follow-up from Hepatitis B Foundation Meetings with US – NIAID, NIDDK and NCI

This session was suggested by HBV Forum steering committee members as an important issue to report to HBV Forum members on the efforts the Hepatitis B Foundation (HBF) had done approaching the US National Institutes of Health (NIH) to prioritize HBV cure research. The session was presented by Dr. Carol Brosgart on behalf of Hepatitis B Foundation/Baruch S. Blumberg Institute.

Participants considered that the session was appropriate in length (78%) and that the information presented was agreed and strongly agreed that increased the understanding of US-NIH position regarding research towards an HBV cure and that it was a valuable component of HBV Forum 4.

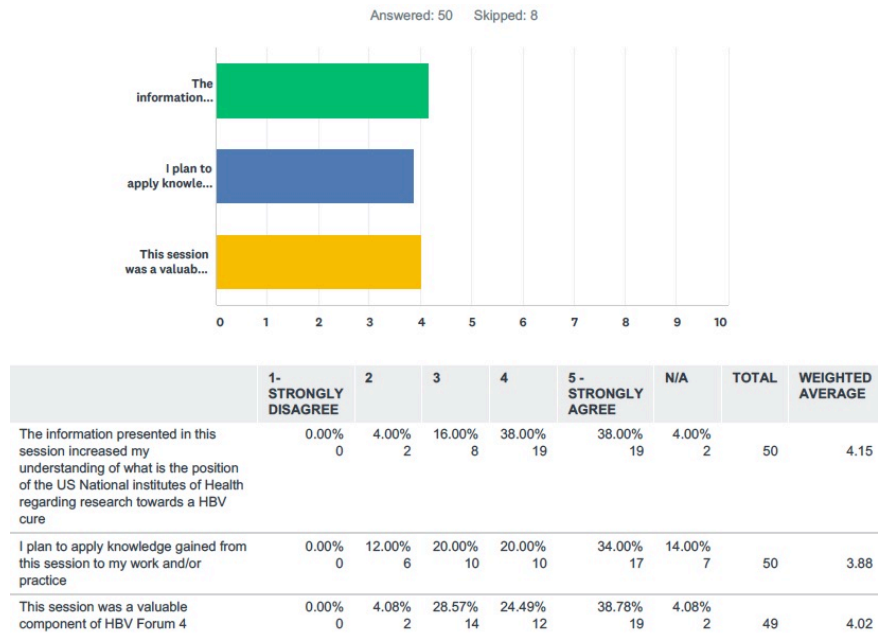


Figure 10: Opinions on Session 7

SESSION 8: HBV Cure Initiatives in the AIDS Clinical Trials Group (ACTG)

Session 8 was presented by Dr. Mark Sulkowski, Medical Director of the Viral Hepatitis Center at Johns Hopkins University and chair, co-chair and investigator in the Clinical Trials Group (ACTG), domestically and internationally. His session focused on presenting the ACTG as a platform to conduct clinical research on HBV in people living with HIV.

The session was considered appropriate in length and very well rated in terms of understanding the different research paths at the ACTG, of applying knowledge gained to professional practice and the value of HBV Forum 4. See Figure 11.

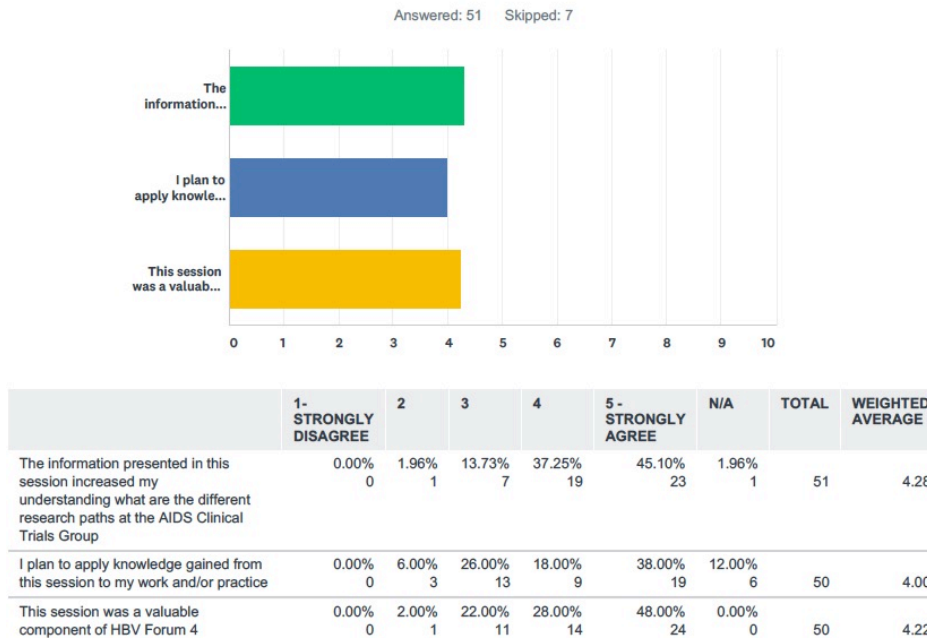
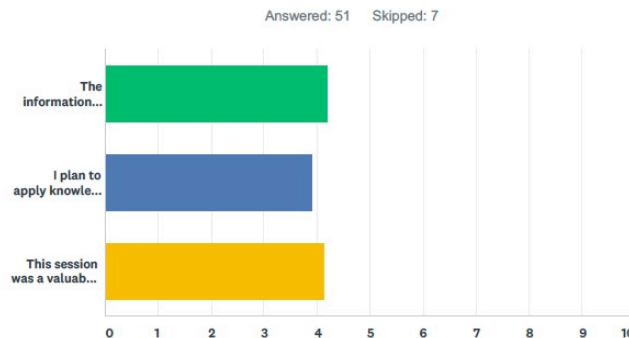


Figure 11: Opinion on Session 8

SESSION 9: Panel Discussion - Community Perspectives on the Road to HBV Cure

Last session a panel comprised of community representatives, advocates and people affected by the epidemic. Present at the panel were HBV Forum Steering Committee members Joan Block and Michael Ninburg and community advocates Maureen Kamischke and Dr. Su Wang.

The session was considered appropriate in length by 73% of respondents, however, more than a fifth of them thought that the session was too long (22%). Nearly half of the respondents strongly agreed that the session contributed to understand the perspectives of the patients and community with regards to HBV cure and less than half strongly agreed that it was a valuable contribution of HBV Forum 4.



	1- STRONGLY DISAGREE	2	3	4	5 - STRONGLY AGREE	N/A	TOTAL	WEIGHTED AVERAGE
The information presented in this session increased my understanding of what are the patients and community perspectives regarding HBV cure	1.96% 1	1.96% 1	19.61% 10	21.57% 11	47.06% 24	7.84% 4	51	4.19
I plan to apply knowledge gained from this session to my work and/or practice	1.96% 1	5.88% 3	19.61% 10	27.45% 14	29.41% 15	15.69% 8	51	3.91
This session was a valuable component of HBV Forum 4	1.96% 1	7.84% 4	11.76% 6	25.49% 13	45.10% 23	7.84% 4	51	4.13

Figure 12: Opinion on Session 9

GENERAL COMMENTS

Participants provided comments and suggestions for the HBV Forum and future meetings. These are some of them.

- Excellent meeting. Well organized program, with appropriate topic prioritization The Forum gets better with every meeting. Keep up the strong work
- Better logistics than in the past for those attending on-line
- Provide a list of current HBV cure and funding projects and project contact details whom interest parties can reach out for collaboration
- The HBV Forum is having a positive effect on improved flexibility on the part of regulators
- It might be helpful to have a community working group. Hopefully there would be others interested in better understanding the barriers patients face living with CHB
- Increase the number and scope of subgroups

How to encourage and facilitate collaboration

- Reduce the number of topics per session. Be more focused
- More updates between meetings

- Get the working groups to be working in a more structured way, involving/informing all members
- Facilitate entry into and participation in working groups
- Sub group independent meeting may facilitate collaboration
- More networking opportunities. Perhaps single topic lectures

Favorite aspects of HBV Forum 4

- Scientific data presentation. Variety of topics covered. In depth updates on research and clinical studies. Collaborative efforts among several diverse groups
- Open the discussion for combination therapy and scientific topics that would advance the field
- The input from Perelson, Gehring and Maini on ways to collect samples, to data collection and indicator of HBV trend
- Session with patient representatives
- Collaboration with ACTG. Updates on government alliances
- Networking. Possibility to meet collaborators in person. Involvement of the regulatory agencies
- Immunology lectures
- Robert Gish's "Roadmap on HBV at EASL 2018 was an excellent initial overview/wrap-up"

Room for improvement from HBV Forum 4

- Distance to the meeting venue and timing of the meeting. Close to another EASL session on the same topic. It needs to be either in the convention center or somewhere within walking distance
- Stick to the agenda. Have longer breaks
- Fewer topics and more time for discussion
- The meeting was unfocused. It was not especially useful or enjoyable
- Discussion seems to be driven by a small handful of people
- Involvement of FDA and EMA

Recommendations for future HBV Forum meetings

- Have at least one meeting outside of EASL/AASLD
- [COMM. REP.] I was grateful for the opportunity to share our stories, which increased networking we have not encountered in past meetings. Hopefully we can do something similar in the future
- More discussions on needed markers
- Allow more time for facilitated discussion (5-10 min) for Q&A after each presentation.

- Allow subgroups to present
- Better projector. Sound was excellent
- Include the NIH/DAIDS Clinical Trials Group (ACTG) again

Suggested additional topics for HBV Forum 5 in San Francisco, California

- Updates on current trials, recent studies and report on interim data analysis
- Role of capsids in the combination with nucleo(s)tide analogs (NA)
- Update on testing diagnostics; point of care testing; any alternatives to HBsAg, more affordable HBV DNA
- What new endpoints should be developed
- Language and semantics of CHB. Goals for HBV: endpoints, treatments, etc. Definitions of cure
- Discussions about minimum functional cure response that is expected with the first finite treatments to become available
- Specific inhibitors
- Pharma/biotech needs in finding suitable HBV patient populations, site development, etc.
- Detailed discussions of the key issues that working groups are covering: 1) flares, 2) agency acceptable endpoints, etc. Maybe fewer presentations and more interaction with working groups
- Enrollment of women in clinical trials. Gender differences in treatment outcomes and how to address the gender unbalance in the field of HBV/Hepatology. How can we still tolerate “male only panels”?
- Have separate working group meetings
- Clinical path to show functional cure (or remission) in the clinical setting. Pragmatic and down-to-earth feedback from clinicians, regulatory agencies and industry
- More basic science, immunology
- Lack of HBV treatment worldwide
- Early markers of HBsAg loss in clinical trials
- Regulatory considerations and constraints for development of novel multi-investigational drug combination therapies for HBV infection: US, EU and international (especially Asian territories)
- Potential companion diagnostics for HBV treatment for therapy stratification and therapy monitoring
- Biomarkers and diagnostics