Forum for Collaborative HIV Research
Advancing HCV Drug Development: A Collaborative Approach
UC Washington Center
1608 Rhode Island Avenue NW
Washington DC 20036
December 6, 2010

	Session 1: DDAs for HCV in Development: Current Status and Need **Moderators: Veronica Miller, PhD, *Forum for Collaborative HIV Research* , and Jeffrey Murray, MD, MPH, *Food and Drug Administration***	
9:00 AM	**Welcome and Introductions** Veronica Miller, PhD, *Forum for Collaborative HIV Research*	0:05
9:05 AM	**Regulatory Perspective** Jeffrey Murray, MD, MPH, *Food and Drug Administration*	0:10
9:15 AM	**Perspective of Professional Societies: AASLD and EASL** Leonard Seeff, MD, *Amercian Association for the Study of Liver Diseases Representative* Jean-Michel Pawlotsky, MD, PhD, *European Association for the Study of the Liver Representative*	0:10
9:25 AM	**Recap of FCHR HCV DRAG Working Group Meetings** Ann Kwong, PhD, *Vertex Pharmaceuticals*	0:10
9:35 AM	**Preclinical Overview: FDA and EMA perspectives** Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies* Peyton Myers, PhD, *Food and Drug Administration*	0:10
	Session 2: General Clinical Design Considerations **Panel Discussion and Public Response** **Facilitator: Jur Strobos, MD, JD, FACEP, *Forum for Collaborative HIV Research***	
9:45 AM	**Panel 2.1**: **Phase 1/2 Trial Design** **Moderator:** Don Jensen, MD, FACP, *University of Chicago* Michelle Berrey, MD, MPH, *Pharmassett, Inc* Laurent Castera, MD, PhD, *University Hospital of Bordeaux* Sarah Connelly, MD, *Food and Drug Administration* Jeffry Florian, PhD, *Food and Drug Administration* Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies* Michal Odermarsky, MD, PhD, *Lund University* Andy Talal, MD, MPH, *Weill Cornell Medical College* 1) What is the recommendation for duration of phase I monotherapy for different classes of agents with different barriers to resistance? 2) In phase II DAA combination studies: a. What will be the requirement for demonstrating safety and efficacy with prior-approved DAA agents? For example, having demonstrated safety and efficacy with an in-house PI/Nuc combo, what will need to be done to combine the Nuc with an "approved" PI? Will safety and efficacy need to be demonstrated with all prior-approved agents? 3) How important is liver biopsy in early phase trials for: a) Efficacy assessment? b) Fibrosis assessment? c) Scientific investigation of antiviral effect? 4) How important is a SOC "tail" in future trial design? What is its role? 5) What will be the role of IL28B, and geno-1a vs. 1b; fibrosis scores: a) For stratification? b) For trial design? 6) After approval of the first DAA, what will be the approach to trial design and resistance considerations in treatment failures? 7) What will be the role of a SOC "lead-in" in future trial design?8)What will be the threshold and barriers to approval for a second-wave DAA agent which does not demonstrate an improvement in efficacy in a triple therapy design but which holds significant promise in combination with another DAA (i.e. a ribavirin effect)? 8) What will be the threshold and barriers to approval for a second-wave DAA agent which does not demonstrate an improvement in efficacy in a triple therapy design but which holds significant promise in combination with another DAA (i.e. a ribavirin effect)?	0:50
10:35 AM	**BREAK**	0:15

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10:50 AM	**Panel 2.2**: **Phase 3 Trial Design** **Moderator:** Kimberly Struble, PharmD, *Food and Drug Administration* Russ Fleischer, PA-C, MPH, *Food and Drug Administration* Filip Josephson, MD, PhD*, Swedish Medical Products & European Medicines Agencies* Michael Ninburg, MPA*, Hepatitis Education Project* Mary Singer, PhD, MD, FACP, *Food and Drug Administration* Mark Sulkowski, MD, *Johns Hopkins University School of Medicine* Brian Woodfall, MD, *Tibotec* 1) Patient Enrollment Criteria. 2) Stratification: Which baseline factors should be considered. 3) Are there any surrogate endpoints for SVR 4) What constitutes appropriate comparator(s) for combination DAA studies with and without SOC 5) Appropriate or acceptable trial designs	0:50
11:40 AM	**LUNCH**	**1:00**
	Session 3: Future Directions for DAAs **Panel Discussion and Public Response** **Facilitator: Nina Mani, PhD, MPH, *Forum for Collaborative HIV Research***	
12:40 PM	**Clinical Overview** Ira Jacobson, MD, *Weill Cornell Medical College*	0:10
12:50 PM	**Panel 3.1**: **Multiple DAA Combination Therapy** **Moderator:** Ira Jacobson, MD, *Weill Cornell Medical College* Patrick Harrington, PhD, *Food and Drug Administration* Don Jensen, MD, FACP, *University of Chicago* Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies* Doug Mayers, MD, *Idenix Pharmaceuticals* Jean-Michel Pawlotsky, MD, PhD, *French National Reference Centre for Viral Hepatitis B, C and Delta, Hopital Henri Mondor* Kimberly Struble, PharmD, *Food and Drug Administration* Tracy Swan, *Treatment Action Group* 1) With recent data presented at AASLD in mind, what are the minimal critieria required for a combination DAA regimen to be put into clinical trials? 2) Might these criteria be altered for interferon-incapable patients (i.e. can the "bar" be made lower)? 3) Should there be a ribavirin-containing arm in all such trials for the foreseeable future? 4) Is there a role for IL28B testing in selecting patients for DAA combination trials? 5) What should the main stratification parameters be in such trials (e.g. genotype 1 subtype; IL28B; degree of fibrosis; ethnicity, etc.). 6) Should DAA combinations be tested in both naive and treatment-experienced patients, or should the focus be on one of these populations? 7) Is 24 weeks after end of treatment still the best time point at which to assess for SVR? 8) Should patients who have failed treatment with a protease inhibitor be included in upcoming DAA combination trials? 9) Safety data required for combination DAA only vs. combination DAA + SOC trials for late phase 2/3 drug development. 10) Other than SVR, can any efficacy endpoint be used to predict viral clearance? 11)Will time to SVR change in combination DAA only therapies and how would it affect trial design? 12) What stopping rules would you incorporate into such trials? 13) How impactful should concerns about resistance be in our formulations (including single vs multiclass resistance)?	0:50
1:40 PM	**HCV Resistance and Remaining Challenges** Jean-Michel Pawlotsky, MD, PhD, *French National Reference Centre for Viral Hepatitis B, C and Delta, Hopital Henri Mondor*	0:10

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1:50 PM	**Panel 3.2**: **Current understanding of HCV resistance and treatment failure with new DAAs** **Moderator:** Jean-Michel Pawlotsky, MD, PhD, *French National Reference Centre for Viral Hepatitis B, C and Delta, Hopital Henri Mondor* Patrick Harrington, PhD, *Food and Drug Administration* Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies* Tara Kieffer, PhD, *Vertex Pharmaceuticals* Jules Levin, *National AIDS Treatment Advocacy Project* Isabel Najera, PhD, *Hoffman La Roche* *Ira Jacobson, MD, Weill Cornell Medical College* 1) Identification of HCV genotypes and subtypes a) how important is it ? b) how can it be accurately determined ? 2) Definitions for treatment failure and patterns 3) Role of DAA resistance in treatment failure 4) Development of predictive algorithms based on baseline and on-treatment parameters a) lead-in phase b) baseline parameters c) practical use 5) Development of database for collaborative studies to monitor HCV drug resistance	0:50
2:40 PM	**BREAK**	0:15
	Session 4 : Unmet Needs in HCV Therapy **Panel Discussion and Public Response** **Facilitator: Veronica Miller, PhD, *Forum for Collaborative HIV Research***	
2:55 PM	**Panel 4.1**: **HIV/HCV Co-infected Patients, Patients with Decompensated Cirrhosis, Liver Transplant, and other Special Populations** **Moderator:** Mark Sulkowski, MD, *Johns Hopkins University School of Medicine* Paul Brayshaw, MPH, *Hemophilia Federation of America* Don Jensen, MD, FACP, *University of Chicago Medical Center* Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies* Jeffrey Murray, MD, MPH, *Food and Drug Administration* Sarah Robertson, PharmD, *Food and Drug Administration* Tracy Swan, *Treatment Action Group* 1) Need for drug-drug interaction data with commonly used drugs in these patients. 2) Minimum safety and efficacy data required to conduct trials in these popualtions, 3) Types of trial designs that can show efficacy in these special patient populations with and without SOC.	0:45
3:40 PM	**Panel 4.2**: **Current Drug Users and Patients in Opiate Substitution Therapy** **Moderator**: Tracy Swan, *Treatment Action Group* Michael Carden, MS, *Weill Cornell Medical College* Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies* Luis Mendao, *European AIDS Treatment Group* Jeffrey Murray, MD, MPH, *Food and Drug Administration* Sarah Robertson, PharmD, *Food and Drug Administration* Susan Whitley, MD, *Kings County Hospital Center* 1) Why is it important to include these populations in DAA trials? 2) When should drug-drug interactions between DAAs and drugs used for opioid substitution treatment be performed? 3) Are there additional interaction studies that should be performed to facilitate safe and effective use of DAAs in these populations? 4) Are there valid reasons for excluding people on OST from participating in DAA trials (aside from uncharacterized drug-drug interactions)? If so, what are they, and what are ways to address concerns?	0:45

5) How can investigators assess which OST patients are good candidates for clinical trials — what are the criteria that really matter?
6) What is the best way to scale up the capacity to conduct clinical trials for people on OST?
7) Where should these trials be conducted?
8) At what stage of development should patients on OST be allowed enrollment in clinical trials? (e.g., phase 2, phase 3, post-approval?)

4:25 PM **Panel 4.3**: **Considerations in Pediatric Populations and Early Access Protocols/Treatment INDs** 0:35
Moderator: Kimberly Struble, PharmD, *Food and Drug Administration*

Lynda Dee, JD, *AIDS Action Baltimore*
Filip Josephson, MD, PhD, *Swedish Medical Products & European Medicines Agencies*
Jules Levin, *National AIDS Treatment Advocacy Project*
Linda Lewis, MD, *Food and Drug Administration*
Michal Odermarsky, MD, PhD, *Lund University*
Kathleen Schwarz, MD, *Johns Hopkins University Pediatric Liver Center & Pediatric Liver Transplant Program*
Mark Sulkowski, MD, *Johns Hopkins University School of Medicine*

1) Discuss the timing of pediatric HCV studies in relation to adult studies.
2) Comment on the timing of expanded access protocols in relation to ongoing trials.
3) Comment on enrollment priorities of special populations.

5:00 PM **WRAP UP** 0:05