

*program*



*& abstracts*



INTERNATIONAL CONFERENCE ON  
VIRAL HEPATITIS



*april 11-12, 2011*



*baltimore*

JOINTLY SPONSORED BY



*This activity is supported by educational grants from Gilead Sciences, Merck & Co., and Vertex Pharmaceuticals.*

# WELCOME

Thank you for joining us for the inaugural International Conference on Viral Hepatitis.

We welcome you to a state-of-the-science forum at which we will examine sound and practical strategies to understand and enhance the clinical management of hepatitis B virus (HBV) and hepatitis C virus (HCV).

There is clearly a need for this conference. We base this assertion on the rapid changes that are occurring in the science of viral hepatitis, and the multifaceted clinical and behavioral issues that hepatologists, gastroenterologists, and HIV-treating clinicians must understand in order to deliver quality HBV and HCV care and treatment.

This conference is an important forum to present the best evidence on HBV and HCV treatment, but the primary reason we come together is to rapidly translate these scientific advances into approaches that can make a difference in real-world settings.

We extend our gratitude to the conference's Planning Committee, the International Association of Physicians in AIDS Care (IAPAC), and the Johns Hopkins School of Medicine's Office of Continuing Medical Education. We also sincerely express our appreciation to the Office of AIDS Research (OAR) at the National Institutes of Health (NIH), and to our commercial supporters, for their financial contributions. Finally, a special thank you to our distinguished faculty for what we are sure to be cutting-edge presentations to help advance our learning objectives.



Mark S Sulkowski, MD<sup>1</sup>  
Co-Chair



Jürgen K Rockstroh, MD, PhD<sup>2</sup>  
Co-Chair

1. Associate Professor, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States

2. Professor, Department of Medicine, University of Bonn, Bonn, Germany

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## ACCREDITATION AND CME INFORMATION

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The International Conference on Viral Hepatitis is jointly sponsored by the Johns Hopkins University School of Medicine, the International Association of Physicians in AIDS Care (IAPAC), and the University of Bonn.

### DESCRIPTION

There exist significant challenges to diagnosing and linking to treatment large numbers of hepatitis B virus (HBV)- and hepatitis C virus (HCV)-infected patients who are unaware of their serostatus and thus are not on either anti-HBV or anti-HCV treatment. Additionally, bottlenecks preventing expanded access to HBV and HCV care must be addressed in light of shifting treatment paradigms, which requires an expanded number of clinicians from multiple disciplines to deliver HBV and HCV care.

Presentations will feature state-of-the-art information on HBV and HCV research, clinical perspectives, and medical treatment, both within the context of HBV and HCV mono-infection, as well as coinfection with HIV. The conference will feature 15 oral abstract presentations, a poster session, plenary presentations, and invited panel discussions.

Clinical management issues to be examined include:

- defining parameters for HBV and HCV treatment success;
- identifying and managing adherence and other behavioral and clinical issues unique to patients with HBV or HCV;
- exploring the importance of preventing HBV and HCV drug resistance; and
- evaluating current data related to new HBV and HCV treatment options and modalities, including direct action antivirals (DAAs) for HCV treatment.

### LEARNING OBJECTIVES

After attending this activity, the participant will demonstrate the ability to:

- Discuss parameters for treatment success in patients who are infected with HBV or HCV
- Describe potential patient adherence issues unique to patients with HBV or HCV
- Examine the importance of preventing HBV resistance and HCV resistance

### INTENDED AUDIENCE

This activity is intended for gastroenterologists, hepatologists, infectious disease (ID) and non-ID-specialized HIV-treating physicians, nurses, and pharmacists.

The Johns Hopkins University School of Medicine takes responsibility for the content, quality, and scientific integrity of this CME activity.

### ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the Johns Hopkins University School of Medicine, International Association of Physicians in AIDS Care (IAPAC), and University of Bonn. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

### CREDIT DESIGNATION STATEMENT

The Johns Hopkins University School of Medicine designates this live activity for a maximum of 8.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

### FACULTY DISCLOSURE

It is the policy of The Johns Hopkins University School of Medicine that the faculty and provider disclose real or apparent conflict of interest relating to the topics of this educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentation(s). Detailed disclosure will be made in made in the conference handout materials.

### DISCLAIMER STATEMENT

The opinions and recommendations expressed by faculty and other experts whose input is included in this activity are their own. Use of Johns Hopkins University School of Medicine name implies review of educational format design and approach.



## ACCREDITATION AND CME INFORMATION

### NOTICE ABOUT OFF-LABEL USE PRESENTATIONS

The International Conference on Viral Hepatitis may include presentations on drugs or devices, or use of drugs or devices, that have not been approved by the Food and Drug Administration (FDA) or have been approved by the FDA for specific uses only. The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or device he or she wishes to use in clinical practice.

The Johns Hopkins University School of Medicine is committed to the free exchange of medical education. Inclusion of any presentation in this program, including presentations on off-label uses, does not imply an endorsement by Johns Hopkins of the uses, products, or techniques presented.

### COMMERCIAL SUPPORTERS

We wish to acknowledge the following companies that have provided educational grants in support of this activity:

- Gilead Sciences
- Merck & Co.
- Vertex Pharmaceuticals

### OTHER SUPPORTERS

The Office of AIDS Research (OAR) at the National Institutes of Health (NIH) provided an educational grant in support of this activity.

### AMERICANS WITH DISABILITIES ACT

IAPAC and the Johns Hopkins University School of Medicine fully comply with the legal requirements of the ADA and the rules and regulations thereof. Please notify us if you have any special needs.

### COPYRIGHT INFORMATION

All rights reserved. No part of this syllabus may be used or reproduced in any manner whatsoever without written permission except in the case of brief quotations embodied in articles or reviews.

### CME CREDIT FOR PHYSICIANS (MDs and DOs)

In accordance with our accreditation guidelines, the Johns Hopkins Office of Continuing Medical Education has instituted a self-reporting system for physicians to obtain *AMA PRA Category 1 Credit™*. To receive a certificate of credit, physicians must attest to the exact number of hours that they have been in attendance.

**A self-report credit form will be available at the Registration Desk. All participants must complete, sign, and return this form to an IAPAC staff member at the Registration Desk on the last day of the activity. Physicians must document the amount of time they spent in the activity.**

All certificates will be emailed to the address attendees include on their self-report credit forms.

### SIGN-IN SHEET FOR ALL PARTICIPANTS

Please be sure to sign in once to verify your attendance. If you have paid for your registration by Hopkins Tuition Remission (TR), you must, per University policy, sign in and/or pick up your name badge at the registration desk to confirm your attendance. If we cannot verify attendance by sign in sheet or badge, we must bill the cost of your registration back to your department as a no show fee (per TR policy).

### ACTIVITY EVALUATION

Activity evaluation forms will be available to attendees to evaluate each session and each speaker's presentation, as well as to identify future educational needs.

### OUTCOMES SURVEY

An outcomes survey will be sent to all physician attendees within three months post activity to assist us in determining what impact this activity had on the attendee's practice.



# DISCLAIMER

## CONFIDENTIALITY DISCLAIMER FOR CME CONFERENCE ATTENDEES

I certify that I am attending a Johns Hopkins University School of Medicine CME activity for accredited training and/or educational purposes.

I understand that while I am attending in this capacity, I may be exposed to "protected health information," as that term is defined and used in Hopkins policies and in the federal HIPAA privacy regulations (the "Privacy Regulations"). Protected health information is information about a person's health or treatment that identifies the person.

I pledge and agree to use and disclose any of this protected health information only for the training and/or educational purposes of my visit and to keep the information confidential.

I understand that I may direct to the Johns Hopkins Privacy Officer any questions I have about my obligations under this Confidentiality Pledge or under any of the Hopkins policies and procedures and applicable laws and regulations related to confidentiality. The contact information is: Johns Hopkins Privacy Officer, telephone: 410-735-6509, e-mail: HIPAA@jhmi.edu.

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**"The Office of Continuing Medical Education at the Johns Hopkins University School of Medicine, as provider of this activity, has relayed information with the CME attendees/participants and certifies that the visitor is attending for training, education and/or observation purposes only."**

For CME Questions, please contact the CME Office (410) 955-2959 or e-mail [cmenet@jhmi.edu](mailto:cmenet@jhmi.edu).  
For CME Certificates, please call (410) 502-9634.

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Reviewed & Approved by:  
General Counsel, Johns Hopkins Medicine (4/1/03)  
Updated 4/09



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**KEYNOTE SPEAKER**

**Barbara McGovern, MD**

Associate Professor of Medicine  
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**PLENARY SPEAKERS**

**Douglas T Dieterich, MD\***

Professor of Medicine  
Mount Sinai School of Medicine  
New York, NY, United States

**Mamta Jain, MD, MPH**

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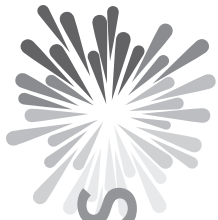
**Kenneth E Sherman, MD, PhD**

Gould Professor of Medicine  
University of Cincinnati College of Medicine  
Cincinnati, OH, United States

**Vincent Soriano, MD, PhD**

Assistant Director of Infectious Diseases  
Complutense University of Madrid  
Madrid, Spain

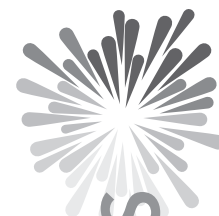
\*Planning Committee



## FULL DISCLOSURE POLICY AFFECTING CME ACTIVITIES

As a provider approved by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of the Johns Hopkins University School of Medicine Office of Continuing Medical Education (OCME) to require signed disclosure of the existence of financial relationships with industry from any individual in a position to control the content of a CME activity sponsored by OCME. Members of the Planning Committee are required to disclose all relationships regardless of their relevance to the content of the activity. Speakers are required to disclose only those relationships that are relevant to their specific presentation. The following relationships have been reported for this activity:

NAME AND LECTURE TITLE(S)	RELATIONSHIP(S)
<p><b>Douglas T Dieterich, MD</b> Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies</p>	<p>Consultant: Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Pharmasset, Roche Laboratories; Honorarium: Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Pharmasset, Roche Laboratories; Grants and consults: Achillion, Boehringer Ingelheim, Gilead Sciences, Pharmasset, Roche Laboratories</p>
<p><b>Mamta Jain, MD, MPH</b> Invited Panel - HCV Drug Resistance: What Does it Mean in Practice?  Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies</p>	<p>Disclosures for both sessions are:  Consultant/research grant: Merck &amp; Co.; Advisor/research grant: Vertex Pharmaceuticals; Research grant: Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Roche Laboratories</p>
<p><b>Marion G Peters, MD</b> Plenary - Overview: Treatment of HBV Infection</p>	<p>Honorarium: Roche Laboratories; Spouse's employer: Genentech</p>
<p><b>Stuart Ray, MD</b> Invited Panel - HCV Drug Resistance: What Does it Mean in Practice? (Moderator)  Late Breaker Oral Abstract Session (Moderator)</p>	<p>Disclosures for both sessions are:  Data Safety Monitoring Committee: Boehringer Ingelheim, Roche Laboratories; Consultant/advisor: Pharmasset</p>
<p><b>Jürgen K Rockstroh, MD, PhD</b> Plenary - Overview: Treatment of HBV Infection</p>	<p>Consultant/honorarium: Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmith-Kline, Merck &amp; Co., Pfizer Inc., Roche Laboratories, Tibotec Therapeutics, ViiV; Research grant/funding: Abbott Laboratories, Merck &amp; Co., Roche Laboratories</p>
<p><b>Kenneth E Sherman, MD, PhD</b> Invited Panel - HCV Drug Resistance: What Does it Mean in Practice?  Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies</p>	<p>Disclosures for both sessions are:  Research grant/funding: Anadys, Bristol-Myers Squibb, Gilead Sciences, Merck &amp; Co., Roche Laboratories, Vertex Pharmaceuticals; Consultant/speaker: SciClone</p>



NAME AND LECTURE TITLE(S) <i>(continued)</i>	RELATIONSHIP(S) <i>(continued)</i>
<b>Mark S Sulkowski, MD</b>	
Plenary - Direct Action Antivirals: What Are They? What Is Their Place in HCV Management?	Disclosures for both sessions are:
Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies	Grants/research consultant: Abbott Laboratories, Boehringer Ingelheim, Gilead Sciences, Merck & Co., Novartis, Pharmasset, Roche Laboratories, Vertex Pharmaceuticals; Advisory Board: Pfizer Inc.
<b>David L Thomas, MD, MPH</b>	
Invited Panel - HCV Drug Resistance: What Does it Mean in Practice?	Disclosures for both sessions are:
Plenary - Using Genetic Markers to Plan for Treatment Success	Advisor: Merck & Co.; Grant/research supplies (no funds): Gilead Sciences, Merck & Co.

No other speakers have indicated that they have any financial interests or relationships with a commercial entity whose products or services are relevant to the content of their presentation(s).

## ORAL ABSTRACT PRESENTERS

NAME AND LECTURE TITLE(S)	RELATIONSHIP(S)
<b>Douglas T Dieterich, MD</b>	
Interim Analysis of a Phase 2a Double-Blind Study of Telaprevir in Combination with Peginterferon Alfa-2a and Ribavirin in HIV/HCV-Coinfected Patients	Consultant: Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Pharmasset, Roche Laboratories; Honorarium: Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Pharmasset, Roche Laboratories; Grants and consults: Achillion, Boehringer Ingelheim, Gilead Sciences, Pharmasset, Roche Laboratories
<b>Vincent Lo Re, MD</b>	
Adherence to Hepatitis C Virus Therapy: Relationship with Virologic Outcomes and Change in Adherence Over Time	Research grant funding: Department of Veterans Affairs, NIH/NIAID
<b>Mark S Sulkowski, MD</b>	
Boceprevir Combined with Peginterferon alfa-2b/Ribavirin for Previous Treatment Failure Patients with Hepatitis C Virus Genotype 1: RESPOND-2 Final Results	Disclosures for both sessions are:
Boceprevir Combined with Peginterferon alfa-2b/Ribavirin for Previously Untreated Patients with Hepatitis C Virus Genotype 1: SPRINT-2 Final Results	Grants/research consultant: Abbott Laboratories, Boehringer Ingelheim, Gilead Sciences, Merck & Co., Novartis, Pharmasset, Roche Laboratories, Vertex Pharmaceuticals; Advisory Board: Pfizer Inc.

No other oral abstract presenters have indicated that they have any financial interests or relationships with a commercial entity whose products or services are relevant to the content of their presentation(s).

## NON-CME ORAL ABSTRACT PRESENTERS

NAME AND LECTURE TITLE(S)	RELATIONSHIP(S)
<b>Richard JO Barnard, PhD</b> Rate of Reemergence of Wild Type Sequence at Boceprevir (BOC) Resistance-Associated Variant (RAV) Loci in HCV Genotype 1a and 1b Patients  Frequencies of Resistance-Associated Amino Acid Variants Following Combination Treatment with Boceprevir (BOC) Plus PEGINTRON (PegInterferon Alfa-2b)	Disclosures for both sessions are:  Employment/salary: Merck & Co.; Ownership interest/stock: Merck & Co.
<b>Claudia Kasserra, PhD</b> Clinical Pharmacology of Boceprevir (BOC): Metabolism, Excretion, and Drug-Drug Interaction	Employment/salary: Merck & Co.; Ownership interest/stock: Merck & Co.

## PLANNERS

NAME	RELATIONSHIP(S)
<b>Douglas T Dieterich, MD</b>	Grants/research consultant: Boehringer Ingelhem, Bristol-Myers Squibb, Gilead Sciences, Idenix, Genentech, Vertex Pharmaceuticals
<b>Marina Nuñez, MD, PhD</b>	Grants/research: Bristol-Myers Squibb, Department of Veterans Affairs, NIH/NIAID
<b>Massimo Puoti, MD</b>	Grants/research: Janssen Cilag, Merck Sharp & Dohme; Consultant: Abbott Laboratories, Gilead Sciences, Merck Sharp & Dohme, Roche Laboratories; Honorarium: Bristol-Myers Squibb, Gilead Sciences, Janssen Cilag, Merck Sharp & Dohme, Novartis, Roche Laboratories
<b>Jürgen K Rockstroh, MD, PhD</b>	Grants/research consultant: Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Merck & Co., Pfizer Inc., Roche Laboratories, Tibotec Therapeutics, Viiv
<b>Mark S Sulkowski, MD</b>	Grants/research consultant: Abbott Laboratories, Boehringer-Ingelhim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Merck & Co., Novartis, Pharmasset, Roche Laboratories, Tibotec Therapeutics, Vertex Pharmaceuticals; Advisory Board: Pfizer Inc.
<b>José M Zuniga, PhD, MPH</b>	Consultant: Bristol-Myers Squibb

**No other planners have indicated that they have any financial interests or relationships with a commercial entity.**

Note: Grants to investigators at the Johns Hopkins University are negotiated and administered by the institution which receives the grants, typically through the Office of Research Administration. Individual investigators who participate in the sponsored project(s) are not directly compensated by the sponsor, but may receive salary or other support from the institution to support their effort on the project(s).



## OFF-LABEL PRODUCT DISCUSSION

The following speakers have disclosed that their presentation will reference unlabeled/unapproved uses of drugs or products:

NAME AND LECTURE TITLE(S)	PRODUCT(S)
<b>Mamta Jain, MD, MPH</b>	
Invited Panel - HCV Drug Resistance: What Does it Mean in Practice?	boceprevir, telaprevir
Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies	boceprevir, telaprevir
<b>Mark R Nelson, MD</b>	
Invited Panel - From Bench to Clinic: Translating Research to Practice in HCV Management	boceprevir, telaprevir
<b>Jürgen K Rockstroh, MD, PhD</b>	
Plenary - Overview: Treatment of HBV Infection	boceprevir, telaprevir
Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies (Moderator)	boceprevir, telaprevir, BMS-790052, BMS-650032, mericitabine, danoprevir, BI201335, alisporivir
<b>Kenneth E Sherman, MD, PhD</b>	
Invited Panel - HCV Drug Resistance: What Does it Mean in Practice?	boceprevir, telaprevir
Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies	boceprevir, telaprevir
<b>Mark S Sulkowski, MD</b>	
Plenary - Direct Action Antivirals: What Are They? What Is Their Place in HCV Management?	boceprevir, telaprevir
Closing Panel - Improving Liver Disease Outcomes: New Drugs, New Strategies	boceprevir, telaprevir
<b>David L Thomas, MD, MPH</b>	
Plenary - Using Genetic Markers to Plan for Treatment Success	boceprevir, telaprevir
Invited Panel - HCV Drug Resistance: What Does it Mean in Practice?	boceprevir, telaprevir

**No other speaker has indicated that he/she will reference unlabeled/unapproved uses of drugs or products.**

NOTE: At the time this syllabus went to press, we had not yet received off-label statements from: Marion G Peters, MD. Every attempt to obtain disclosure will be made prior to the meeting/activity. Once disclosure is obtained, we will notify all attendees at the time of the meeting/activity. ACCME regulations prevent us from providing CME credits for any lecture given by a member of the faculty who fails to disclose.

## GENERAL INFORMATION

### MEETING VENUE

The International Conference on Viral Hepatitis is being held at the Grand Historic Venue (attached to the Tremont Plaza Hotel). The Plenary Addresses, Oral Abstracts Sessions, and Invited Panels will take place in the Corinthian Room on the 2nd Floor. The Poster Session will take place in the Doric Room on the 4th Floor.

### MEALS

Your registration to the conference includes continental breakfast and lunch on Monday, April 11, 2011, and only breakfast on Tuesday, April 12, 2011. Both breakfast and lunch will be served in the Marble Room, which is located on the 1st Floor. Morning and afternoon coffee and snack breaks will also be provided in the Doric Room on the 4th Floor.

### INTERNET ACCESS

The Grand Historic Venue and Tremont Plaza Hotel provide complimentary wireless Internet in all guest and public spaces.

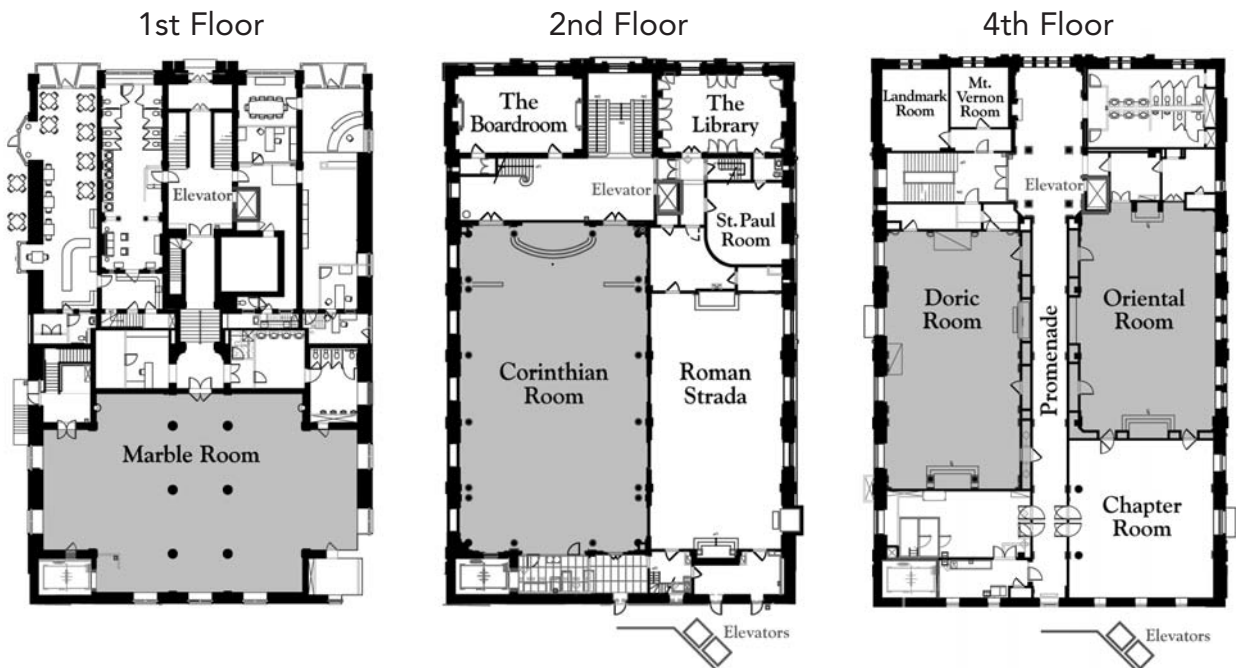
### SLIDE PRESENTATIONS/ABSTRACTS

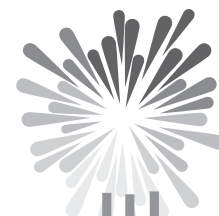
Slide presentations will be available at [www.iapac.org](http://www.iapac.org) post-conference. The Program and Abstracts Book distributed at registration will also be available in electronic format at [www.iapac.org](http://www.iapac.org) post-conference.

### QUESTIONS

If you have any questions during the conference, please locate an IAPAC staff member by leaving a message at the Registration Desk. If you have any questions post-conference, please contact IAPAC Director of Programs Steve Ketchum at [sketchum@iapac.org](mailto:sketchum@iapac.org) or (312) 795-4934.

## GRAND HISTORIC VENUE – FLOOR PLANS





## MONDAY, APRIL 11, 2011

TIME	ACTIVITY
9:00-9:30 A.M.	<b>PLENARY 1</b> <b>Overview: Treatment of HBV Infection</b> Marion G Peters, MD
9:30-10:00 A.M.	<b>PLENARY 2</b> <b>Overview: Treatment of HCV Infection</b> Jürgen K Rockstroh, MD, PhD
10:00-10:30 A.M.	<b>KEYNOTE ADDRESS</b> <b>Impact of Viral Hepatitis in the Era of Potent ART</b> Barbara McGovern, MD
10:30-11:00 A.M.	BREAK - <i>Doric Room (4th Floor)</i>
11:00-11:30 A.M.	<b>ORAL ABSTRACT SESSIONS</b> <b>Session 1: HBV/HCV Clinical Management</b> Moderator: Mark R Nelson, MD
11:30 A.M.-Noon	<b>Session 2: Investigational Agents/ New Strategies</b> Moderator: Karine Lacombe, MD, PhD
Noon-12:30 P.M.	<b>Session 3: HBV/HCV Clinical Management</b> Moderator: Marina Nuñez, MD, PhD
12:30-1:00 P.M.	<b>Session 4: Investigational Agents/ New Strategies*</b> Moderator: Jürgen K Rockstroh, MD, PhD
1:00-2:00 P.M.	LUNCH - <i>Marble Room (1st Floor)</i>
2:00-2:30 P.M.	<b>PLENARY 3</b> <b>Is Liver Biopsy the Gold Standard?</b> Mamta Jain, MD, MPH
2:30-3:00 P.M.	<b>PLENARY 4</b> <b>Acute HCV in HIV-Infected Men: The "New" STD</b> Emma Page, MD
3:00-3:30 P.M.	BREAK - <i>Doric Room (4th Floor)</i>

\*This Oral Abstract Session is **not** accredited for CME.

TIME	ACTIVITY
3:30-4:00 P.M.	<b>PLENARY 5</b> <b>Using Genetic Markers to Plan for Treatment Success</b> David L Thomas, MD, MPH
4:00-5:30 P.M.	<b>INVITED PANELS (Consecutive)</b> <b>From Bench to Clinic: Translating Research to Practice in HCV Management</b>  Moderator: Vincent Soriano, MD, PhD  Panelist 1: Barbara McGovern, MD Panelist 2: Gregory Lucas, MD, PhD Panelist 3: Mark R Nelson, MD  <b>HCV Drug Resistance: What Does it Mean in Practice?</b>  Moderator: <b>Stuart Ray, MD</b>  Panelist 1: Kenneth E Sherman, MD, PhD Panelist 2: David L Thomas, MD, MPH Panelist 3: Mamta Jain, MD, MPH
5:30 P.M.	ADJOURN
5:30-6:30 P.M.	<b>OPENING RECEPTION</b> <i>(Oriental Room, 4th Floor)</i>

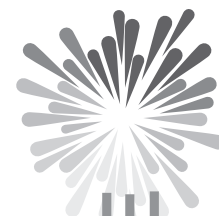


**PROGRAM AT-A-GLANCE**

**TUESDAY, APRIL 12, 2011**

TIME	ACTIVITY
9:00-9:30 A.M.	<b>PLENARY 6</b> <b>Direct Action Antivirals: What are They? What is their Place in HCV Management?</b> Mark S Sulkowski, MD
9:30-10:00 A.M.	<b>PLENARY 7</b> <b>The Aging Liver: Considerations in the HAART Era</b> Douglas T Dieterich, MD
10:00-10:45 A.M.	<b>POSTER SESSION</b> <i>Doric Room (4th Floor)</i>
10:45-11:15 A.M.	BREAK - <i>Doric Room (4th Floor)</i>
11:15-11:45 A.M.	<b>LATE-BREAKER ABSTRACT SESSION</b> Moderator: Stuart Ray, MD
11:45 A.M.-Noon	BREAK (Transition)
Noon-1:00 P.M.	<b>CLOSING PANEL</b> <b>Improving Liver Disease Outcomes: New Drugs, New Strategies</b>  Moderator: Jürgen K Rockstroh, MD, PhD  Panelist 1: Kenneth E Sherman, MD Panelist 2: Mamta Jain, MD, MPH Panelist 3: Douglas T Dieterich, MD Panelist 4: Barbara McGovern, MD  Discussant: Mark S Sulkowski, MD
1:00 P.M.	ADJOURN



**MONDAY, APRIL 11, 2011****Oral Abstract Session 1  
Integrating Adherence Monitoring into  
Clinical Care**

11:00 A.M. - 11:30 A.M.

Moderator: Mark R Nelson, MD

- 70670 **HAART Mitigates Liver Disease Progression in HIV/Viral Hepatitis-Coinfected Men**  
*Jennifer Price presenting*
- 70921 **Adherence to Hepatitis C Therapies and the Impact of Comorbid Conditions**  
*Mary Cassler presenting*
- 71151 **Adherence to Hepatitis C Virus Therapy: Relationship with Virologic Outcomes and Change in Adherence Over Time**  
*Vincent Lo Re presenting*

**Oral Abstract Session 2  
Investigational Agents/New Strategies**

11:30 A.M. - Noon

Moderator: Karine Lacombe, MD, PhD

- 70550 **Factors Associated with Sustained Virological Response to pegIFN-RBV Therapy in IL28B rs12979860 Non-CC HCV/HIV-Coinfected Patients**  
*Pablo Barreiro presenting*
- 70690 **Broader Influence of IL28B Gene Polymorphisms and Interferon  $\lambda$ 3 Plasma Levels on HCV Outcomes in HIV-Infected Patients**  
*Norma I Rallón presenting*
- 71319 **Boceprevir Combined with Peginterferon alfa-2b/Ribavirin for Previous Treatment Failure Patients with Hepatitis C Virus Genotype 1: RESPOND-2 Final Results**  
*Mark S Sulkowski presenting*

**Oral Abstract Session 3  
HBV/HCV Clinical Management**

Noon - 12:30 P.M.

Moderator: Marina Nuñez, MD, PhD

- 70920 **Non-Cirrhotic Portal Hypertension (NCPH): A Serious Hepatic Complication in HIV and the Use of Transient Elastography to Aid in its Diagnosis**  
*Deepti Dronamraju presenting*
- 70965 **Liver Fibrosis is Associated with Increased Oxidative Stress in HIV/HCV-Coinfected Adults**  
*Marianna K Baum presenting*
- 71277 **High Risk of Liver Fibrosis and Cirrhosis among HIV/HBV-Coinfected Persons in Rakai, Uganda**  
*Lara Stabinski presenting*

**Oral Abstract Session 4  
Investigational Agents/New Strategies**

12:30 P.M. - 1:00 P.M.

Moderator: Jürgen K Rockstroh, MD, PhD

- 71320 **Rate of Reemergence of Wild Type Sequence at Boceprevir (BOC) Resistance-Associated Variant (RAV) Loci in HCV Genotype 1a and 1b Patients: Interim Analysis of Long-Term Follow-Up of Patients Treated With Boceprevir + Pegylated-Interferon(IFN) +/- Ribavirin (RBV)**  
*Richard JO Barnard presenting*
- 71323 **Clinical Pharmacology of Boceprevir (BOC): Metabolism, Excretion, and Drug-Drug Interactions**  
*Claudia Kasserra presenting*
- 71327 **Frequencies of Resistance-Associated Amino Acid Variants Following Combination Treatment with Boceprevir (BOC) Plus PEGINTRON (PegInterferon Alfa-2b) and Ribavirin (P/R) in Patients With Chronic Hepatitis C (CHC), Genotype 1 (G1)**  
*Richard JO Barnard presenting*

*This Oral Abstract Session is **not** accredited for CME.***TUESDAY, APRIL 12, 2011****Late-Breaker Abstract Session**

11:15 A.M. - 11:45 A.M.

Moderator: Stuart Ray, MD

- 71227 **Healthcare Utilization and Mortality Associated with HIV and HCV: How to Address the Burden of Liver Disease**  
*Susanna Naggie presenting*
- 71283 **Interim Analysis of a Phase 2a Double-Blind Study of Telaprevir in Combination with Peginterferon Alfa-2a and Ribavirin in HIV/HCV-Coinfected Patients**  
*Douglas T Dieterich presenting*
- 71306 **Boceprevir Combined with Peginterferon alfa-2b/Ribavirin for Previously Untreated Patients with Hepatitis C Virus Genotype 1: SPRINT-2 Final Results**  
*Mark S Sulkowski presenting*



## 70550 Factors Associated with Sustained Virological Response to pegIFN-RBV Therapy in IL28B rs12979860 Non-CC HCV/HIV-Coinfected Patients

Pablo Barreiro (presenting)

Hospital Carlos III, Madrid, Spain

**Methods:** Patients recruited in the PERICO trial, a two-arm randomized trial of pegIFN $\alpha$ -2a 180  $\mu$ g/week plus either RBV 1,000-1,200 mg/day or 2,000 mg/day conducted in HCV/HIV-coinfected patients naïve to IFN $\alpha$  were evaluated. Pre-emptive EPO was administered during the first 4 weeks in the RBV 2,000 mg/day arm. Patients who had completed the entire course of therapy and 6 months thereafter and had IL28B CT/TT genotypes were examined.

**Results:** A total of 68 IL28B CT/TT patients were assessed (75% males; mean age 43 years; 95% on HAART; 89% with plasma HIV-RNA <50 copies/mL; mean CD4 count 660 cells/ $\mu$ l; 96% HCV-G1/4; 73% with baseline HCV-RNA >500,000 IU/mL; 49% Metavir F3-F4; high RBV dosing in 45%. In the on-treatment analysis, SVR was attained by 30% of patients (28% vs 68% for G1/4 vs G2/3 [ $p = 0.2$ ]; 26% vs 46% for baseline HCV-RNA > vs <500,000 IU/mL [ $p = 0.1$ ]; 15% vs 46% for Metavir  $\geq$  vs <F3 [ $p = 0.01$ ]; 20% vs 39% for high vs standard RBV dosing [ $p = 0.1$ ]. Mean baseline triglycerides were 84 vs 118 mg/dL in patients with and without SVR [ $p = 0.03$ ]. No differences were found in plasma RBV trough concentrations at week 4 (2.2 vs 2.1  $\mu$ g/mL [ $p = 0.8$ ]). The number of patients with haemoglobin declines from baseline to week 4 above 2 gr/dL were 82% vs 54% in patients with vs without SVR [ $p = 0.04$ ]. In the multivariate analysis, hemoglobin decline >2 g/dL (OR 7.1 [95% CI, 1.0-48.3],  $p = 0.04$ ) was the only predictor of SVR.

**Conclusions:** In HCV/HIV-coinfected patients with unfavourable IL28B genotypes, a greater haemoglobin decline is associated with SVR to pegIFN $\alpha$ -RBV therapy. This observation supports the important role of RBV exposure and is against the use of pre-emptive EPO to ameliorate RBV-associated anemia, as it may hamper treatment efficacy due to enhanced RBV sequestration by erythrocytes.

## 70670 HAART Mitigates Liver Disease Progression in HIV/Viral Hepatitis-Coinfected Men

Jennifer Price<sup>1</sup> (presenting), Eric C Seaberg<sup>2</sup>, Sheila Badri<sup>3</sup>, Mallory D Witt<sup>4</sup>, Kristin D'Acunto<sup>5</sup>, Chloe Thio<sup>6</sup>

<sup>1</sup> Johns Hopkins University, Baltimore, MD, United States

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<sup>3</sup> John H Stoger, Jr. Hospital of Cook County, Rush University Medical Center, Ruth M. Rothstein CORE, Chicago, IL, United States

<sup>4</sup> David Geffen School of Medicine at UCLA, Los Angeles Biomedical Research Institute at Harbor-UCLA, Los Angeles, CA, United States

<sup>5</sup> University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, United States

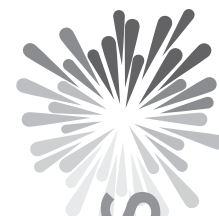
<sup>6</sup> Johns Hopkins University School of Medicine, Baltimore, MD, United States

**Background:** HIV infection accelerates liver fibrosis in individuals co-infected with chronic HBV or HCV not on highly active antiretroviral therapy (HAART). This study aimed to determine the effect of HAART on liver disease progression in HIV/hepatitis coinfection.

**Methods:** Using men enrolled in the Multicenter AIDS Cohort Study, we compared liver disease progression among HIV+ men who initiated HAART to HAART-naïve HIV+/- men over three years. Liver disease was quantified using the AST to platelet ratio index (APRI), which was determined 1 year pre- and 2 years post-HAART initiation and at calendar-time-matched points for HAART-naïve men. Using men with APRI  $\leq 1.5$  at baseline, the annual rate of APRI change was compared using linear regression adjusting for age, alcohol, race, and baseline APRI.

**Results:** 1,755 men were included: 1,148 uninfected, 496 HIV-monoinfected (HIV), 69 HBV- or HCV-monoinfected (Hep), and 42 HIV/hepatitis-coinfected (HIV-Hep). Median age was 45, 74% were Caucasian, 39% drank  $\geq$  modest alcohol, and 0.9% used injection drugs. At baseline, median APRI was highest for the coinfecting (0.81), followed by HIV-monoinfected (0.41), hepatitis-monoinfected (0.41) and uninfected (0.27) ( $p = 0.0001$  across groups). Overall, APRI was stable with a mean change of 0.0068 (+/- 0.0044) points/year. Using multivariate regression, the APRI change compared to the uninfected was 0.05, 0.05, and 0.14 points/year greater for the HIV, Hep, and HIV-Hep groups, respectively ( $p \leq 0.001$  for each comparison) after adjusting for HAART use. Among men with HIV, HIV-Hep was associated with a 0.095 points/year greater APRI change compared to the HIV group ( $p = 0.021$ ) adjusting for HAART. Among men with hepatitis, HIV-Hep HAART-naïve men had a 0.156 points/year higher APRI change compared to Hep men ( $p = 0.02$ ). In contrast, the APRI change in HIV-Hep HAART initiators was not significantly different compared to Hep men ( $p = 0.482$ ) and was 0.114 points/year lower than in HIV-Hep HAART-naïve men ( $p = 0.11$ ).

**Conclusion:** In HIV/hepatitis-coinfected men, two years of HAART reduced liver disease progression by approximately 75%. Thus, HAART substantially diminishes, but does not fully overcome, the accelerated liver disease progression in HIV/hepatitis-coinfected patients.



## 70690 Broader Influence of IL28B Gene Polymorphisms and Interferon $\lambda$ 3 Plasma Levels on HCV Outcomes in HIV Patients

Norma I Rallón (presenting), José M Benito, Pablo Barreiro, Eugenia Vispo, Pablo Labarga, Sonia Rodriguez-Novoa, Vincent Soriano

Hospital Carlos III, Madrid, Spain

**Introduction:** Strong genetic determinants of the natural history and treatment response have recently been unveiled for HCV infection. The impact of IL28B SNPs on the rate of spontaneous clearance and on interferon susceptibility has been reproduced in the HIV population. Moreover, new effects of IL28B alleles on HCV outcomes have been recognized in this population.

**Description:** Analysis of several studies we recently conducted in which distinct HCV-related variables were examined in HIV/HCV-coinfected patients according to IL28B (IFN- $\lambda$ 3) rs12979860 SNPs. A further study assessing IFN- $\lambda$ 3 plasma levels in coinfecting individuals was similarly evaluated.

**Lessons Learned:** The findings of all these studies show the following: The rs12979860 CC genotype exerts a protective effect on both HCV spontaneous clearance and the probability of sustained virological response (SVR) to pegIFN $\alpha$  RBV, mainly in patients infected with HCV genotypes 1 and 4; the CC genotype increases the rate of rapid virological response (RVR) and early virological response (EVR) in patients infected with HCV genotypes 1 and 4, due to faster viral kinetics during the first weeks of therapy; the CC genotype is associated to higher rates of liver cirrhosis and liver inflammation in this population; patients with the C allele harbor higher levels of serum HCV-RNA; and although there are no significant differences in plasma levels of IFN- $\lambda$ 3 (IL28B) when comparing CC and non-CC carriers at baseline, IFN- $\lambda$ 3 is significantly up-regulated after 4 weeks of IFN $\alpha$  RBV therapy only in CC carriers.

**Recommendations:** HIV/HCV-coinfected individuals harboring the rs12979860 allele C could hypothetically display a lower activity of endogenous IFN $\alpha$ , allowing higher HCV replication and liver inflammation while keeping an enhanced susceptibility to exogenous IFN $\alpha$  therapy. These findings have clear implications for the management of HCV-induced liver disease in HIV/HCV-coinfected patients, supporting implementation of IL28B testing as part of routine care of this population.

## 70920 Non-Cirrhotic Portal Hypertension (NCPH): A Serious Hepatic Complication in HIV and the Use of Transient Elastography to Aid in its Diagnosis

Deepti Dronamraju (presenting), Marie Louise Vachon, Douglas T Dieterich

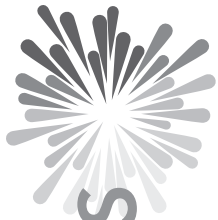
Mount Sinai Medical Center, New York, NY, United States

**Background:** Non-cirrhotic portal hypertension (NCPH) is a rare clinical syndrome that has been recently described in HIV-seropositive patients. The described cases have been associated with the use of the nucleoside reverse transcriptase inhibitor didanosine (ddl). NCPH may be missed due to its subtle presentation in the absence of exposure to other viral hepatitides.

**Method:** This is an observational, retrospective case series of HIV-seropositive patients with portal hypertension without HBV or HCV attending a university liver clinic between 02/2008 and 09/2010.

**Results:** Sixteen (16) patients had portal hypertension. Nine (56%) were men; median age was 48 years (range 41-60); median duration of infection was 18 years (range 13-25); median CD4+ T-cell nadir was 193 cells/mm<sup>3</sup> (range 12-383); median CD4+ T-cell at diagnosis was 377 cells/mm<sup>3</sup> (range 73-658); and HIV RNA was <48 copies/ml in all but one. Median ALT and AST levels were 44 (range 22-104) and 56 (range 17-98), respectively. Manifestations of portal hypertension included thrombocytopenia (platelet count <150,000/mm<sup>3</sup>) in 12/16 (median of 92 with range 42-199); splenomegaly in 13/16; esophageal varices in 13/16; and ascites in 5/16. Of the 16, 5 had portal vein thrombosis. 12 patients had a cirrhotic appearing liver on imaging. Of these 12, 10 underwent transient elastography with a median score of 8.4 kPa (range 4.7-27.7), values not consistent with cirrhosis. Liver biopsy was performed in 9/16 patients: 3/8 had hepatoportal sclerosis (HPS), 2 also had features of nodular regenerative hyperplasia (NRH). One biopsy showed only NRH. Only 1 patient had biopsy-proven cirrhosis.

**Conclusion:** Portal hypertension was not due to cirrhosis in all but one patient. Though imaging suggested cirrhosis, transient elastography helped exclude cirrhosis as the cause of portal hypertension. Biopsy confirmed this as well. Clinicians must be aware of NCPH in the HIV positive population. We propose a definition of NCPH using signs of portal hypertension, like splenomegaly and thrombocytopenia <110,000 plus a fibroscan score less than 15. This may obviate the need for liver biopsy diagnosis of NRH or HPS.



## 70921 Adherence to Hepatitis C Therapies and the Impact of Comorbid Conditions

Mary Cassler (presenting)

Medco Health Solutions, Inc., Franklin Lakes, NJ, United States

**Background:** Studies have shown that patients with chronic hepatitis C must maintain adherence rates of 80%-85% or higher to their hepatitis C virus (HCV) therapies in order to suppress the virus. Common side effects of these therapies make it challenging to attain these adherence levels. Depression and other comorbidities also affect adherence. A claims analysis was performed to evaluate adherence patterns among HCV patients in a managed care setting.

**Methods:** A national pharmacy benefit manager (PBM) claims database was used to identify patients new to HCV therapies receiving interferon (IFN) and ribavirin (RBV). A one-year review period was used to monitor patients' claims and calculate their medication possession ratio (MPR). Adherence to therapy was defined as MPR  $\geq$ 80%. Comorbidities such as HIV and depression were evaluated to determine their impact on patients' adherence to HCV therapies.

**Results:** Of 3,607 HCV-infected patients identified, 1,657 (45.9%) were being treated for depression and 109 (3%) were coinfecting with HIV. Of the patient subset with HIV, 66 also had depression. 60.4% of all patients were adherent to their HCV medications. Patients receiving treatment for depression had the highest adherence rates to HCV medications: 61.5% (depression only) and 69.7% (depression and HIV).

**Conclusions:** 40% of patients do not achieve the adherence rates associated with HCV suppression and therefore risk the development of medication resistance and disease progression. Analysis of a large PBM claims database indicated that patients who were concurrently receiving antidepressant medications demonstrated higher adherence to HCV therapies. This observation emphasizes the value of identifying and appropriately treating patients with depression. Careful monitoring is particularly warranted in patients with HCV, especially considering the established link between IFN therapy and the onset of depressive symptoms. Effective depression screening by healthcare professionals may be a valuable tool to improve treatment adherence in patients with HCV.

## 70965 Liver Fibrosis is Associated with Increased Oxidative Stress in HIV/HCV-Coinfected Adults

Marianna K Baum<sup>1</sup> (presenting), Dushyantha T Jayaweera<sup>2</sup>, Adriana Campa<sup>1</sup>, Victor J Casillas<sup>2</sup>, Sabrina S Martinez<sup>1</sup>, Dong-Ho Shin<sup>1</sup>, Yinghui Li<sup>1</sup>, Sandra Young<sup>3</sup>

<sup>1</sup> Florida International University, Miami, FL, United States

<sup>2</sup> University of Miami, Miami, FL, United States

<sup>3</sup> Jackson Memorial Hospital, Miami, FL, United States

**Background:** The main feature of chronic HCV infection is a progressive liver fibrosis leading to cirrhosis. Oxidative stress activates hepatic stellate cells and corresponds with the severity of the inflammatory histopathological findings. While many studies confirm the presence of elevated oxidative stress in HIV and HCV mono-infections, limited data are available for HIV/HCV coinfection. The objective of this study was to assess the association between oxidative stress and liver fibrosis in HIV/HCV-coinfected adults in Miami.

**Methods:** A cross-sectional study was conducted with 15 HIV/HCV-coinfected adults who have undergone liver biopsy. Upon consenting, blood was collected for measures of oxidative stress (mitochondrial specific 8-hydroxy-deoxyguanosine [mt-specific 8-oxo-dG], malondialdehyde [MDA], reduced, oxidized and total glutathione); HCV viral load. Fibrosis and inflammation were assessed with liver biopsy and scored using the Metavir Liver Fibrosis Scale. Descriptive statistics and Linear Regression statistical analyses were used.

**Results:** Mean age was  $49.53 \pm 6.14$  years and 60% were male. Increased liver fibrosis was significantly associated with increased amount of mt-specific 8-oxo-dG,  $\hat{\alpha} = 1.39$ ,  $p = 0.056$ . The grade of inflammation was positively and strongly associated with oxidized (GSSG) glutathione ( $\hat{\alpha} = 0.0034$ ,  $p = 0.002$ ). GSSG/Total glutathione was also positively associated with grade of inflammation,  $\hat{\alpha} = 0.0275$ ,  $p = 0.05$ . There was no significant relationship between MDA and liver inflammation grade or fibrosis stage. However, MDA was positively associated with HCV viral load ( $\hat{\alpha} = 2.4$ ,  $p = 0.041$ ).

**Conclusions:** In this relatively small study, we found strong associations between the extent of liver damage and the measures of oxidative stress in HIV/HCV-coinfected patients. These data support our hypothesis that oxidative stress increases with the severity of liver disease in HCV-coinfected, HIV-seropositive patients. Studies that supplement antioxidants to HIV/HCV-coinfected patients to reduce oxidative stress as a potential antifibrotic target are needed.



## 71151 Adherence to Hepatitis C Virus Therapy: Relationship with Virologic Outcomes and Change in Adherence Over Time

Vincent Lo Re (presenting), Valerie Teal, Russell Localio, Valerianna Amorosa, David Kaplan, Robert Gross

University of Pennsylvania, Philadelphia, PA, United States

**Background:** Adherence to hepatitis C virus (HCV) therapy with pegylated interferon (PEG-IFN) and ribavirin has been incompletely examined. Our objectives were to evaluate the relationship between adherence to HCV therapy and early (EVR) and sustained virologic response (SVR) and assess changes in adherence over time.

**Methods:** We conducted a retrospective cohort study among HCV-infected patients treated with PEG-IFN and ribavirin in the National VA Hepatitis C Clinical Case Registry. Eligible subjects had: 1) HCV genotype 1-4; 2) at least one prescription for PEG-IFN plus ribavirin between 2003 and 2006; 3) a quantitative HCV viral load prior to therapy; and 4) a viral load after treatment initiation. Adherence to each medication was calculated over 12-week intervals using pharmacy refill data. Endpoints included EVR (decrease of  $>2 \log_{10}$  HCV RNA at 12 weeks) and SVR (undetectable HCV RNA 24 weeks after end of treatment). Logistic regression estimated associations between adherence and EVR and SVR, by genotype. Mixed effects models estimated mean changes in adherence over time.

**Results:** Among 5,706 treated chronic HCV patients, EVR increased with higher levels of ribavirin adherence over the initial 12 weeks of therapy (genotype 1, 4: 25/68 [37%] with the lowest category [ $<40\%$  adherence] versus 1,367/2,187 [63%] with the highest category [91-100% adherence],  $p < 0.001$ ; genotype 2, 3: 12/18 [67%] with  $<40\%$  adherence versus 651/713 [91%] with 91-100% adherence,  $p < 0.001$ ). Among genotype 1 and 4 patients, SVR increased with higher ribavirin adherence over the second, third, and fourth 12-week intervals. Results were similar for PEG-IFN adherence. Mean adherence to PEG-IFN and ribavirin decreased 3.5% and 6.8% per 12-week interval, respectively (test for trend,  $p < 0.001$  for each drug).

**Conclusions:** EVR and SVR increased with higher levels of adherence to PEG-IFN and ribavirin. Adherence to both antivirals declined over time, but more so for ribavirin.

## 71227 Healthcare Utilization and Mortality Associated with HIV and HCV: How to Address the Burden of Liver Disease

Susanna Naggie<sup>1</sup> (presenting), Lawrence P Park<sup>1</sup>, Ziad Gellad, Kevin Schulman<sup>1</sup>, Charles Hicks<sup>1</sup>, John McHutchison<sup>2</sup>, Andrew Muir<sup>1</sup>

<sup>1</sup> Duke University/Duke Clinical Research Institute, Durham, NC, United States

<sup>2</sup> Gilead Sciences, Foster City, CA, United States

**Background:** The impact of HCV infection on the U.S. healthcare system will peak in the next decade. Due to shared routes of transmission, many HIV-1-infected patients are HCV co-infected. Understanding trends and reasons for hospitalization in HIV/HCV-coinfected and mono-infected patients will inform future resource allocation.

**Methods:** Data was obtained from the Nationwide Inpatient Sample (NIS) between 1994 and 2007. HIV and HCV observations were identified by ICD9 code. Reason for hospitalization was determined from primary and secondary discharge diagnosis codes. Multivariable models were used for adjusted analyses. All results are adjusted for NIS sample weights and using the US Consumer Price Index for Medical Care.

**Results:** Over the course of the study, crude annual hospitalizations for HIV-1-infected patients declined by 30%, while for HCV and coinfected patients the number increased 10.3- and 9.2-fold, respectively. Similarly, changes in total healthcare spending, which over the course of the study decreased in HIV mono-infected patients from 3.67 billion to 3.2 billion, but increased from 627 million to 6.9 billion and 63 million to 655 million in HCV mono-infected and coinfected patients, respectively. Factors associated with higher healthcare costs included HIV, HCV, and HIV/HCV coinfection ( $P < 0.0001$ ,  $P < 0.0001$ ,  $P = 0.0474$ ), increased age ( $P < 0.0001$ ), male gender ( $P < 0.0001$ ), and in-hospital death ( $P < 0.0001$ ). All-cause mortality decreased over time for all groups. Factors associated with mortality (adjusted OR [95% CI]) included: HIV (2.3 [2.2, 2.4]); HIV/HCV (2.0 [1.9, 2.1]); HCV (1.6 [1.6, 1.7]); female gender (0.77 [0.76, 0.78]); and public insurance carrier (1.2 [1.1, 1.2]).

**Conclusions:** HIV infection remains a leading cause of hospitalization and death, but rates are declining in the era of improved antiretroviral therapy. In contrast, healthcare utilization is dramatically increasing for HCV-mono-infected and HIV/HCV-coinfected persons. These data confirm previous modeling reports of increasing healthcare resource burden in patients with HCV infection.



## 71277 High Risk of Liver Fibrosis and Cirrhosis among HIV/HBV-Coinfected Persons in Rakai, Uganda

Lara Stabinski<sup>1</sup> (presenting), Gregory D Kirk<sup>2</sup>, Steven J Reynolds<sup>1</sup>, Ponsiano Ocama<sup>3</sup>, Francis Bbosha<sup>4</sup>, Valerian Kiggundu<sup>4</sup>, Melissa Saulynas<sup>2</sup>, Oliver Laeyendecker<sup>1</sup>, Ron Gray<sup>2</sup>, Maria Wawer<sup>2</sup>, David L Thomas<sup>2</sup>, Tom Quinn<sup>1</sup>, Chloe Thio<sup>2</sup>

- <sup>1</sup> National Institutes of Health, Bethesda, MD, United States
- <sup>2</sup> Johns Hopkins University, Baltimore, MD, United States
- <sup>3</sup> Makerere University, Kampala, Uganda
- <sup>4</sup> Rakai Health Sciences Program, Kampala, Uganda

**Background:** In resource-limited settings, limited data exist on the effects of HIV coinfection on hepatitis B (HBV)-related liver fibrosis. We assessed factors associated with significant liver fibrosis in an HIV/HBV-coinfected population in Rakai, Uganda.

**Methods:** Liver fibrosis was assessed by transient elastography (FibroScan) in 61 HIV/HBV-coinfected and 51 HBV-monoinfected participants with fibrosis or cirrhosis defined using prior validated cut-offs ( $\geq 9.3$  or  $\geq 12.3$  kPa, respectively). Modified Poisson regression was used to estimate prevalence rate ratios (PRR) of factors associated with fibrosis.

**Results:** HIV/HBV subjects were older than HBV subjects (median age, 37 [IQR, 32-43] and 30 yrs [25-39], respectively,  $P = 0.002$ ) ~50% of both groups were male. The median ALT was 25 and 24 U/L in the HIV-HBV and HBV groups, respectively. 54% of HIV/HBV subjects were receiving antiretroviral therapy (ART) with lamivudine. A majority of HIV/HBV patients on ART had HBV DNA levels below the limit of detection (60%), with HBV only (50%) and HIV/HBV not on ART (20%). The prevalence of significant fibrosis and cirrhosis was higher among HIV/HBV subjects (28% and 16%) than HBV only subjects (14% and 2%;  $p = 0.069$  and  $p = 0.011$ , respectively). Adjusting for age, gender, and alcohol use and compared to HBV only subjects, HIV/HBV coinfection was associated with a 2.3-fold (95% CI 1.0-5.0) and 10.7-fold (95% CI 1.3-91.0) increased risk of significant fibrosis and cirrhosis, respectively. When evaluated by ART status and CD4 nadir, only those HIV/HBV subjects not yet on ART exhibited an increased risk of fibrosis, (PRR 2.7 [1.2 -6.5] & 5.0 [1.8-13.9] for CD4 nadir  $\geq 200$  and  $< 200$  cells/mm<sup>3</sup>, respectively). Among all subjects, even after adjusting for HIV, CD4 nadir and ART, detectable HBV DNA  $> 100$  IU/ml remained a risk factor for fibrosis (PRR 2.7 [1.1-6.7]). In the HIV/HBV population, ART appeared to reduce fibrosis risk by ~60% (PRR 0.4 [0.1-1.0]).

**Conclusions:** In Uganda, HIV coinfection increases the risk for significant liver disease. Higher HBV DNA, lower CD4 nadir, and absence of ART increase liver disease risk, underscoring the need for effective treatment for both HIV and HBV in resource-limited settings.

## 71283 Interim Analysis of a Phase 2a Double-Blind Study of Telaprevir in Combination with Peginterferon Alfa-2a and Ribavirin in HIV/HCV-Coinfected Patients

Douglas T Dieterich<sup>1</sup> (presenting), Jürgen K Rockstroh<sup>2</sup>, Kenneth E Sherman<sup>3</sup>, Nathalie Adda<sup>4</sup>, Lisa Mahnke<sup>4</sup>, Varun Garg<sup>4</sup>, Shahin Gharakhanian<sup>4</sup>, Scott McCallister<sup>4</sup>, Vincente Soriano<sup>5</sup>, Mark S Sulkowski<sup>6</sup>

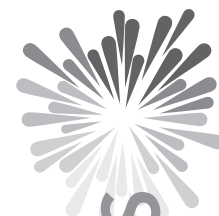
- <sup>1</sup> Mount Sinai School of Medicine, New York, NY, United States
- <sup>2</sup> University of Bonn, Bonn, Germany
- <sup>3</sup> University of Cincinnati School of Medicine, Cincinnati, OH, United States
- <sup>4</sup> Vertex Pharmaceuticals, Cambridge, MA, United States
- <sup>5</sup> Hospital Carlos III, Madrid, Spain
- <sup>6</sup> Johns Hopkins University, Baltimore, MD, United States

**Background:** In the era of effective antiretroviral therapy (ART), HCV disease is a major cause of morbidity and mortality in HIV-infected patients (pts). We investigated the safety, viral kinetics and efficacy of treatment with telaprevir (TVR) and PegIFN- $\alpha 2a$ /RBV in HIV/HCV genotype 1-coinfected interferon-naïve pts: Part A, no concurrent ART; Part B, stable, predefined ART with TDF/FTC with either EFV or ATV/r. The results of a planned interim analysis are reported.

**Methods:** Pts in each part were randomized into: 1) TVR 750 mg q8h + PegIFN- $\alpha 2a$  180  $\mu$ g/wk + RBV 800 mg/day for 12 wks followed by 36 wks of PegIFN- $\alpha 2a$  + RBV (TVR/PR groups) and 2) Placebo + PegIFN- $\alpha 2a$ /RBV for 48 wks. TVR dose was 1125mg q8h when the ART regimen included EFV.

**Results:** This interim analysis was performed on 59 of the 60 dosed pts (Part A, 13; Part B, 46). Overall, 88% were male, 69% white, mean age was 46 yrs, 68% had genotype 1a, 83% baseline HCV RNA  $> 800,000$  IU/mL and 10% advanced liver fibrosis based on liver biopsy. RVR, cEVR and eRVR results are shown in the table. Two pts in Part B experienced HCV viral breakthrough. Discontinuations due to AEs occurred in 2 pts (3%) in the TVR/PR groups versus 0 in the placebo group. Pruritus, nausea, vomiting, fever, anorexia and dizziness were more frequent in pts who received TVR/PR than in controls. No case of severe rash was seen. No significant changes in CD4 decrease or in HIV RNA level were observed in part B pts who received either ART regimen compared to controls.

**Conclusions:** In this interim analysis, substantially more pts receiving a TVR-based regimen achieved undetectable HCV RNA at wks 4 and 12. The safety and tolerability of TVR/PR was consistent with that previously observed in HCV-monoinfected pts; no novel AEs were detected. The study is ongoing for assessment of SVR.



## 71306 Boceprevir Combined with Peginterferon alfa-2b/Ribavirin for Previously Untreated Patients with Hepatitis C Virus Genotype 1: SPRINT-2 Final Results

Mark S Sulkowski<sup>1</sup> (presenting), Fred Poordad<sup>2</sup>, Jonathan McCone Jr<sup>3</sup>, Bruce R Bacon<sup>4</sup>, Savino Bruno<sup>5</sup>, Michael P Manns<sup>6</sup>, Ira M Jacobson<sup>7</sup>, K Rajender Reddy<sup>8</sup>, Zachary D Goodman<sup>9</sup>, Navdeep Boparai<sup>10</sup>, Vilma Sniukiene<sup>10</sup>, Clifford A Brass<sup>10</sup>, Janice K Albrecht<sup>10</sup>, and Jean-Pierre Bronowicki<sup>11</sup> for the SPRINT-2 Investigators

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**Background:** Peginterferon/ribavirin represents the current standard of care for chronic hepatitis C virus (HCV). Sustained virologic response (SVR) has been below 50% in genotype 1. Boceprevir is a potent oral HCV-protease inhibitor.

**Methods:** SPRINT-2 was a double-blind, randomized study of previously untreated adults with HCV genotype 1 assessing a 4-week lead-in with peginterferon alfa-2b plus ribavirin, followed by: (1) peginterferon/ribavirin/ placebo for 44 weeks (standard therapy); (2) peginterferon/ribavirin/boceprevir for 24 weeks, with an additional 20 weeks of peginterferon/ribavirin/placebo if HCV RNA was detected between Weeks 8-24 (response-guided therapy); or (3) peginterferon/ribavirin/boceprevir for 44 weeks (48-week therapy). Non-black (Cohort 1) and black (Cohort 2) patients were enrolled/analyzed separately.

**Results:** A total of 938 non-black and 159 black patients were treated. In Cohort 1, SVR was achieved in 125/311 (40%) patients with standard therapy, 211/316 (67%) with response-guided therapy ( $p < 0.001$ ), and 213/311 (68%) with 48-week therapy ( $p < 0.001$ ); Cohort 2 SVR was 23%, 42% ( $p = 0.044$ ), and 53% ( $p = 0.004$ ). In Arm 2, 47% of patients received 28-week therapy. Anemia was common on boceprevir. Erythropoietin was used in 24% of controls and 43% of boceprevir recipients. Anemia led to dose reductions in 13% of controls and 21% of boceprevir recipients, with discontinuations in 1 and 2%.

**Conclusions:** Boceprevir with peginterferon/ribavirin significantly increased SVR over standard therapy. Overall responses were comparable with response-guided therapy (24 weeks of boceprevir with peginterferon/ribavirin for 28 or 48 weeks) and 48-week therapy.

## 71319 Boceprevir Combined with Peginterferon alfa-2b/Ribavirin for Previous Treatment Failure Patients with Hepatitis C Virus Genotype 1: RESPOND-2 Final Results

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**Background:** Outcomes are suboptimal after retreatment of patients with genotype 1 chronic hepatitis C (HCV) infection who were nonresponders or relapsers after prior peginterferon/ribavirin therapy.

**Methods:** To assess the effect of adding boceprevir, a protease inhibitor that binds to the HCV-NS3 active site, to peginterferon/ribavirin for retreatment of genotype 1 nonresponders and relapsers, we randomly assigned patients (1:2:2) to one of three arms. Each received a 4-week lead-in with peginterferon alfa-2b/ribavirin. Arm 1 ( $n = 80$ , control), then received placebo plus peginterferon/ribavirin for 44 weeks, Arm 2 ( $n = 162$ ) received boceprevir plus peginterferon/ribavirin for 32 weeks and those with detectable HCV-RNA at week 8 received an additional 12 weeks of peginterferon/ribavirin, and Arm 3 ( $n = 161$ ) received boceprevir plus peginterferon/ribavirin for 44 weeks. Primary endpoint was sustained virologic response (SVR, undetectable HCV-RNA levels 24 weeks post-treatment).

**Results:** Rates of SVR in both boceprevir arms were significantly higher than control: 21.3%, 58.6% and 66.5% in Arms 1, 2 and 3 ( $P < 0.001$ ). Those with undetectable HCV-RNA by week 8 had SVR rates of 86.5% and 88.1% with 32 and 44 weeks of triple therapy. Of 102 patients with a  $< 1\text{-log}_{10}$  decrease in HCV-RNA at treatment week 4, SVR were 0%, 32.6% and 34.1% in Arms 1, 2 and 3. The incidence of anemia was higher on receiving boceprevir (43-47%), compared with control (20%), and erythropoietin was used in 41-46% of boceprevir-treated patients and 21% of controls.

**Conclusions:** Addition of boceprevir to peginterferon/ribavirin achieved significantly higher rates of SVR in relapsers and nonresponders to previous peginterferon/ribavirin therapy.



## 71320 Rate of Reemergence of Wild Type Sequence at Boceprevir (BOC) Resistance-Associated Variant (RAV) Loci in HCV Genotype 1a and 1b Patients: Interim Analysis of Long-Term Follow-Up of Patients Treated With Boceprevir + Pegylated Interferon(IFN) +/- Ribavirin (RBV)

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**Background:** To assess the persistence of resistance associated amino acid variants (RAVs) in non-SVR patients that received BOC plus IFN +/- RBV, patients with detectable RAVs at the end of therapy were enrolled in a 3-year follow-up study.

**Methods:** HCV RNA was quantified by Taqman (Roche) and NS3 RAVs were detected by population sequencing (Virco BVBA). Using Kaplan-Meier analysis, the rate and median time of return of wild type (WT) sequence at each BOC resistance loci was determined in subjects with majority RAVs (detected in >25% of subjects) V36M, T54S or R155K in patients with genotype 1a virus and T54S and T54A in patients with genotype 1b virus.

**Results:** 183/307 non-SVR patients that received BOC had a minimum of 2-years of follow-up data available. These 183 patients had G1a or G1b viruses that developed RAVs during treatment and which were still detectable at end of therapy. In total, RAVs were followed at a total of 11 boceprevir resistant loci; namely V36, Q41, F43, T54, V55, R155, A156, V158, I/V170. Median time to reemergence of WT sequence was shortest for G1b viruses with T54A (0.24 yrs); reemergence of WT in viruses with T54S was longer in both G1a and G1b (median time 1.46 and 1.21 yrs, respectively). In G1a, median time to reemergence of WT was shortest for V36M, 0.78 yrs, compared with 1.28 yrs for the R155K variant.

**Conclusion:** WT at each RAV loci re-emerged at different rates depending on the specific RAV selected; WT re-emerged most rapidly in genotype 1a or 1b viruses with T54A and V36M, as compared to viruses with either T54S or R155K. Variation in the appearance of resistance and rates of re-emergence of WT at each loci reflects relative fitness of the specific RAVs in the specific genetic background.

## 71323 Clinical Pharmacology of Boceprevir (BOC): Metabolism, Excretion, and Drug-Drug Interactions

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**Background:** BOC is a HCV NS3 protease inhibitor for treatment of chronic hepatitis C.

**Methods:** Phase 1 multiple-dose studies were conducted in healthy subjects to study: (1) the pathways used in BOC metabolism/elimination, and (2) drug interactions, using medications likely to be coadministered in HCV patients.

**Results:** **BOC Exposure:** No clinically relevant changes in BOC exposure observed when coadministered with peginterferon (PEG) alfa-2b, tenofovir (TFV), or drosiprenone (DRSP) + ethinyl estradiol (EE). A slight reduction in BOC AUC(0-8h) and  $C_{max}$  and a 44% decrease in BOC  $C_{min}$  observed when coadministered with efavirenz (EFV). Ketoconazole (KCZ) increased BOC exposure; however, ritonavir and clarithromycin had minimal effects on steady-state BOC exposure. Coadministration of diflunisal or ibuprofen had little effect on the steady-state exposure to BOC. A dose of 14C-radiolabeled BOC was metabolized to one primary ketone-reduced metabolite; radioactivity in urine and feces accounted for 9% and 79% of the dose, respectively. **Exposure of Coadministered Drugs:** No clinically relevant change in PEG2b exposure seen during BOC coadministration. BOC had no effect on TFV AUC or renal clearance, but increased TFV  $C_{max}$  by 32%. BOC slightly increased EFV AUC(0-24h) and  $C_{max}$ ; increased DRSP AUC(0-24h) and  $C_{max}$ ; and decreased EE AUC (24%) with no effect on EE  $C_{max}$ . Midazolam (MDZ) plus steady-state BOC resulted in increased MDZ exposure: 177%  $C_{max}$  and 430% AUC0-24 h.

**Conclusions:** Data suggest CYP3A4 and P-gp do not contribute substantially to BOC metabolism/elimination; increased exposure to BOC with KCZ suggests involvement of another non-CYP3A4-mediated pathway. The increase in MDZ supports BOC as a strong, reversible inhibitor of CYP3A4. Radiolabeled data support a primarily hepatic-mediated clearance of BOC. No BOC dosage adjustment is needed with coadministration of PEG2b or TFV. The clinical implications of reduced BOC trough concentration when coadministered with EFV are unclear. Finally, BOC administration should not reduce contraceptive efficacy.



# 71327

## Frequencies of Resistance-Associated Amino Acid Variants Following Combination Treatment with Boceprevir (BOC) Plus PEGINTRON (PegInterferon Alfa-2b) and Ribavirin (P/R) in Patients With Chronic Hepatitis C (CHC), Genotype 1 (G1)

Richard JO Barnard (presenting), Lisa D Pedicone, Eirum Chaudhri, Xiao Tong, Ping Qiu, Clifford A Brass, Janice K Albrecht, Patricia Mendez, Robert Ralston

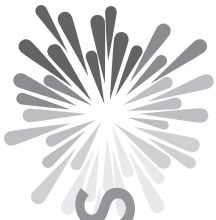
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**Background:** BOC added to P/R leads to high rates of sustained viral response (SVR) in CHC G1 patients. We evaluated treatment-naïve CHC G1 patients who received BOC/P/R in a Phase 2 trial open-label trial (SPRINT-1) to determine factors associated with frequency of resistance-associated variants (RAVs).

**Methods:** 595 patients were randomized to a control arm of P/R for 48 wks or one of 5 BOC treatment arms. HCV-RNA was detected using Roche Taqman. Amino acid variants at BOC resistance loci in the NS3/4A protease were detected using population sequencing.

**Results:** SVR was significantly higher in all BOC arms compared to control. Of 595 patients, 401 were HCV G1a and 188 were G1b. Of 109 patients who developed RAVs on-study, 78 were G1a, 30 were G1b and 1 could not be sub-typed. The most frequently detected on-study RAVs in G1a patients were R155K, V36M, and T54S whereas the most frequently detected in G1b patients were T54S, T54A, A156S, and I170A. Among the 109 patients that developed RAVs on-study, 2 achieved SVR and 107 were non-responders, relapsers or breakthroughs. Over 90% of subjects experiencing virologic breakthrough and 26% who experienced virologic relapse had RAVs detected on-study. Patients randomized to low dose R had the highest frequency of on-study RAVs whereas those assigned 4 wk P/R lead-in followed by 44 week BOC/P/R had the lowest frequency. Notably, 24/595 patients had known RAVs at baseline, and the majority achieved SVR. Among the 3 most frequent RAVs, T54S was observed less frequently in patients receiving lead-in therapy.

**Conclusions:** The profiles of on-study RAVs differed between G1a and G1b patients. As in prior studies, the most common RAVs in G1a patients not achieving SVR were V36M, T54S and R155K. Despite having RAVs at baseline, the majority of such patients achieved SVR.



## 69307 Effects of Fluoroquinolones on the Helicase Activity of HCV NS3 Protein

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**Background:** Hepatitis C virus (HCV) has infected an estimated over 170 million individuals worldwide. Effective therapy against HCV is still lacking. There is a desperate need therefore to develop new treatment against this virus. Current evolution in the field of HCV has come from two major discoveries: construction of Con1, a genotype 1b replicon that is able to independently replicate in the cell line Huh 8, and the development of a cell culture model, using Huh 7 cells transfected with synthetic HCV RNA, to produce virions that are also infectious. Fluoroquinolones inhibit bacterial DNA replication by targeting the enzymes gyrase and topoisomerase IV. These drugs have also been shown to have inhibitory activity against some viral helicases. In the present study, we have used the above-mentioned HCV culture models to test the activity of fluoroquinolones against HCV.

**Methodology:** Huh 7 cells producing the HCV virion as well as actively dividing Huh 8 cells were grown in the presence or absence of over 10 different fluoroquinolone antibiotics for either 72 or 96 hours. Afterwards, Both Huh 7 and Huh 8 cells were lysed, and viral RNA was extracted. The extracted RNA was reverse transcribed and quantified by real-time qPCR using primers against HCV gene NS3.

**Results:** To varying degrees, all of the tested fluoroquinolones effectively inhibited HCV replication in Both Huh 7 and Huh 8 models.

**Conclusions:** The two HCV culture models can be effectively used for the development of novel therapeutics and vaccines against HCV. Fluoroquinolones hold a great deal of promise for treatment against HCV infection.

## 70517 Occult Hepatitis B & C in HIV-Infected Patients

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**Background:** Prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) occult infection has not been described in HIV-infected patients in India. The objective of this study was to assess the prevalence of occult HBV & HCV infection in HIV positive sexually acquired transmission risk group.

**Methods:** 100 sexually acquired HIV-positive patients were taken up for the study of occult HBV/HCV coinfection. Data on demographics, sexual behaviour, sexually transmitted diseases (STD), medical history, laboratory tests viz., serum ALT and CD4 count were recorded. HCV serology included anti-HCV & HCV RNA (RT-PCR).

**Results:** Occult HBV infection (HBV DNA) was observed in 6% (6/100 with HBsAg -ve subjects) while an overall prevalence of HBV DNA was 13% (6% occult & 7% in HBsAg+ve patients). The Occult HCV infection was detected 2 out of 58 (2%) individuals. The HBV/HCV-coinfected group (n = 15) showed a significantly high ALT (214.3 + 212.3 U/l) & low CD4 count (200.5 + 29.7 cells/mm<sup>3</sup>). The percent prevalence of HBV/HCV coinfection was higher in the lower literacy group, in men less than 30 years of age, and in those who were married.

**Conclusions:** The study demonstrated that in HIV-infected patients testing only serological viral markers like HBsAg, antiHBcIgG & anti HCV, fails to identify the true prevalence of coinfection with HBV and HCV. Qualitative PCR for HBV DNA & HCV RNA detects coinfection in patients who are negative for serological markers.



## 70538 Assessment of Psychosocial Readiness for HCV Treatment

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**Introduction:** Treatment for hepatitis C virus (HCV) infection with a combination of weekly injections of pegylated-interferon and daily oral ribavirin has high rates of physical and neuropsychiatric side effects which lead to nonadherence and early treatment discontinuation. Pre-treatment evaluation which identifies psychosocial factors that potentially interfere with treatment adherence can result in recommendations for interventions to optimize treatment outcomes.

**Description:** The HCV Psychosocial Readiness Assessment Tool (HCV-PRAT) was developed in response to the lack of guidelines and scarcity of screening tools to meet clinicians' needs. The HCV-PRAT provides an initial screening of a patient's psychosocial readiness to begin HCV treatment and leads to recommendations and referrals to increase treatment preparedness. It assesses nine areas of psychosocial functioning: Motivation; Hepatitis C Health Literacy; Medication Adherence; Self-Efficacy; Social Support and Stability; Alcohol and Substance Use; Psychiatric Stability; Reading Ability, and Cognitive Functioning and Fatigue. These domains, posited to relate to HCV treatment adherence, are rated as "Satisfactory"; "Could Be Improved"; or "Needs Further Evaluation" as a way to guide clinicians' decision making and identify domains that would benefit from immediate intervention and/or referral for further evaluation or intervention. Interview length varies from 30-45 minutes based on the interviewer's skill level and on the patient's degree of psychosocial complexity. It has been translated into Spanish.

**Lessons Learned:** The HCV-PRAT has been used over the last year to evaluate 30 patients and has undergone continual revision during this pilot process. Ten service providers from diverse disciplines have been trained in administration and are currently using it in clinical practice. Recommendations: Web-based training should be established to more widely disseminate the HCV-PRAT. Preliminary validation efforts should focus on feasibility and utility of administration. Evaluation from both providers and patients should be elicited. It should be adapted to the new generation of HCV treatments coming.

## 70562 Hepatotoxic Effects Associated with Antiretroviral Therapy in Ghanaian Adults Infected with Human Immunodeficiency Virus and the Role of Hepatitis B or C Virus Infection

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**Background:** Highly active antiretroviral therapy (HAART) has been shown to significantly suppress HIV infection and improve CD4 counts in patients with HIV/AIDS. However toxicities linked to the use of antiretroviral drugs has limited its use especially in resource limited country like Ghana.

**Method:** Hospital based prospective cohort study, over a 30-month period. 382 patients were followed up after consecutive sampling from January 2006 to June 2008. Each patient was screened for HBV and HCV at initiation of ART and followed up periodically for 24 weeks. Subjects were closely monitored for hepatotoxic events; defined as an increase in ALT/AST levels to four or five times the upper limit of normal and an increase of at least 100 U/L from baseline.

**Results:** The mean age was 39 years (SD±9); 66% were females; 353 (92.4%) patients had WHO stages III and IV disease. The baseline mean CD4 cell count was 109 cells/mm<sup>3</sup>. 28.8% of patients had CD4 <50 cells/mm<sup>3</sup>. 50% of this cohort was on lamivudine (3TC) and stavudine (d4T), and 47.4% zidovudine (ZDV) and 3TC as a combination drug and 10 (2.6%) subjects were on other combinations. Ninety-six percent were on an NNRTI-based regimen. 44% of the patients were on efavirenz (EFV) and 52.9% were on nevirapine. 14.1% developed severe hepatotoxicity out of which 20.4% had hepatitis B and/or C and 16 (7.4%) had HIV mono-infection. The cumulative frequency of all grades of hepatotoxicity were 15.2% (SE = 0.017), 15.7% (SE = 0.018), 16.2% (SE = 0.018) and 18.8% (SE = 0.20) at weeks 4, 8, 12 and 24. In univariate analysis, the presence of HBsAg and/ or HCV Ab (RR 3.705; 95% CI = 2.096 to 6.548 P <0.0001) and the use of d4T (RR 1.133; CI 0.999-1.285 P <0.0005), were the most significant risk factors for hepatotoxicity. Other risk factors were older subject (>42yr RR 1.038 CI = 0.935-1.154 p = 0.0026), female sex (1.035 CI = 0.950-1.128) and alcohol use (alcohol RR 1.157 CI = 0.969-1.381).

**Conclusions:** It is recommended that standardized antiretroviral regimens for developing country settings should consider potential liver toxicity and capabilities for monitoring of this toxicity to prevent morbidity, mortality, and treatment discontinuation in HIV-infected patients.



## 70586 In Vitro Selectivity Studies Comparing HCV Protease Inhibitor Telaprevir and HIV Protease and Reverse Transcriptase Inhibitors

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**Background:** The combination of pegylated-interferon-alfa (P), ribavirin (R), and telaprevir (TVR), a potent hepatitis C (HCV) NS3-4A protease inhibitor, has shown significantly improved sustained virologic response rates in genotype 1 HCV-monoinfected patient trials. Patients coinfecting with HIV and HCV constitute ~10% (4.5 million) of HIV-infected patients worldwide; these patients show a more rapid progression of HCV disease compared to HCV-monoinfected patients. As the selectivity profile of antivirals may have clinical impact in coinfecting patients, prior to evaluating TVR/PR in these patients, we investigated the in vitro selectivity of TVR and HIV-specific inhibitors.

**Methods:** Using HPLC and spectrofluorometry, we quantified the effect of (1) TVR on HIV-1 protease-catalyzed cleavage of an HIV protease substrate and (2) HIV protease inhibitors on HCV NS3-catalyzed cleavage of a peptide substrate. HIV nucleoside reverse transcriptase inhibitors (NRTI) and HIV protease inhibitors were tested for specificity against viral replication using a cell-based HCV replicon assay and an infectious HIV assay.

**Results:** TVR did not inhibit HIV-1 protease activity in vitro (IC<sub>50</sub> >10 micromolar). The HIV protease inhibitors indinavir, saquinavir, ritonavir, atazanavir and darunavir did not inhibit HCV NS3 protease activity (K<sub>i</sub> values >40 micromolar), while nelfinavir, tipranavir and lopinavir were relatively weak inhibitors (K<sub>i</sub> values 8 to 24 micromolar) compared to TVR (K<sub>i</sub> = 0.044 micromolar). The HIV NRTIs tenofovir, emtricitabine, lamivudine, and PIs ritonavir and atazanavir showed little to no inhibition of HCV replication (IC<sub>50</sub> 22.95 to >30 micromolar) compared to TVR (IC<sub>50</sub> of 0.47 micromolar). The activity of TVR against HIV-1/IIIB and cytotoxicity in MT4 cells was 15.34 and 16.04 micromolar, respectively.

**Conclusions:** Telaprevir, a specific and selective inhibitor of HCV replication, did not inhibit HIV replication in vitro. Similarly, HIV-specific inhibitors did not show significant in vitro inhibition of HCV NS3 protease or replication. The clinical evaluation of telaprevir in HIV/HCV-coinfecting patients is ongoing.

## 70601 Liver Fibrosis Progression in HIV-Infected Patients in the HAART Era: Role of Comorbidities and Antiretroviral Drugs

Pablo Barreiro (presenting)

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**Background:** Liver disease is a leading cause of complications in HIV-infected individuals. Availability of non-invasive tools to measure liver fibrosis allows assessment in large numbers of patients.

**Methods:** A prospective cohort of HIV-infected individuals was established in 2004, when hepatic transient elastometry (TE) was introduced. In subjects with a second TE ≥18 months after the first one, factors associated with significant liver fibrosis progression (SLFP) were evaluated. SLFP was defined as increase from ≤ to >9.5kPa and/or ≥30% increase in liver stiffness if >9.5kPa at first evaluation.

**Results:** A total of 632 HIV-infected individuals (mean age; 45-years-old; 78% males; 62% IDUs; mean BMI 24 kg/m<sup>2</sup>; mean CD4 count 546 cells/μL; detectable HCV-RNA 73%; positive HBsAg 8%; alcohol abuse 9%; 85% on HAART) were included. Mean lag between TE was 26.2 months. Baseline >9.5kPa was found in 192 (30%) patients. Overall, 96 (15%) experienced SLFP. In multivariate analysis, a positive serum HCV-RNA was the only predictor of SLFP in the whole study population (OR, 2.83 [1.58-5.05], p <0.01). A longer history of didanosine exposure was associated with SLFP in patients with ≤9.5kPa at baseline (OR, 1.14 [1.03-1.27], p = 0.01) or without chronic hepatitis C (OR, 1.31 [1.12-1.52], p <0.01). A trend towards an association between SLFP and older age (OR, 1.03, 0.99-1.07], p = 0.08) and treatment with NNA (OR, 0.58 [0.33-1.05], p = 0.07) was found in the whole population.

**Conclusions:** SLFP in HIV-infected individuals in the HAART era is mainly associated with chronic hepatitis C. In HCV-negative individuals, prolonged prior didanosine exposure is also significantly associated with SLFP.



## 70632 Interferon-Stimulated Genes (ISGs) are Differentially Expressed According to Treatment Response but not According to IL28b Genotype in Patients with Chronic Hepatitis C Coinfected with HIV

Norma I. Rallón<sup>1</sup> (presenting), Luis A López-Fernández<sup>2</sup>, Clara Restrepo<sup>1</sup>, Maria I García<sup>2</sup>, Vincent Soriano<sup>1</sup>, José M Benito<sup>1</sup>

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<sup>2</sup> Hospital Gregorio Marañón, Madrid, Spain

**Background:** Baseline up-regulation of interferon-stimulated genes (ISGs) in the liver of HCV-monoinfected patients has been associated to pegIFN $\alpha$ -RBV treatment failure. Likewise, IL28B genotypes CT/TT have been associated to poor treatment response. Herein, we examine the gene expression profile in HIV/HCV-coinfected patients with distinct IL28B genotypes and different treatment outcomes following pegIFN $\alpha$ -RBV therapy.

**Methods:** Gene expression profiles were examined in PBMCs from 19 HIV/HCV-coinfected patients using the human whole genome Agilent microarray platform. All patients had completed a course of Peg-IFN $\alpha$ /RBV therapy with validated outcomes. The IL28B SNP rs12979860 was genotyped using the 5' nuclease assay with allele specific TaqMan probes. Patients were split out into four groups according to treatment response (sustained virological response, SVR; non-response, NR) and IL28B genotypes (CC or CT/TT): 5 SVR/CC, 4 SVR/non-CC, 5 NR/CC and 5 NR/non-CC. The GeneSpringGX software was used to select genes differentially expressed by IL28B genotype and treatment response.

**Results:** All patients were on HAART with undetectable plasma HIV-RNA. There were no significant differences in terms of age, HCV-RNA, HCV genotype or CD4 counts when comparing the different groups. Global gene expression profiles showed 80 genes differentially expressed in SVR vs NR patients and 158 differentially expressed in CC vs CT/TT carriers. Gene ontology analysis of genes selected by SVR reveals immune response as one of the biological process over-represented. Most of them were up-regulated in NR. Interestingly, some of these genes were ISGs such as MX1, IFI44, IFI44L, IRF5, IFI6, IFIT3, RSAD2, XAF1 and IFIT1. With respect to the IL28B genotype, immune response genes were also over-represented but unexpectedly ISGs were not differentially expressed in CC vs CT/TT carriers.

**Conclusion:** The baseline expression of ISGs is associated with pegIFN $\alpha$ -RBV treatment response regardless IL28B genotypes. Thus, the beneficial effect of the IL28B CC genotype on treatment outcome is not mediated by a modulation of ISG expression.

## 70636 Impact of HCV Treatment Initiation on Total Medication Burden and Adherence to Concurrent Medications

Maria Pizzirusso (presenting), Jeffrey Weiss, Cory Head

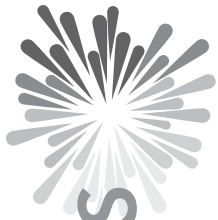
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**Background:** Treatment for HCV is complex given the regimen, toxic side effects, and frequent addition of medications to manage side effects. No data have been published on whether the introduction of HCV treatment negatively impacts adherence to existing regimens. The current study addresses this question in a prospective cohort of patients initiating HCV treatment.

**Methods:** 78 patients (46 HCV; 32 HIV/HCV) beginning HCV treatment were enrolled in the study. 56/78 had longitudinal adherence data [80.4% male; mean age = 51.9 (SD = 11.1)]. Adherence to all medications was assessed at treatment baseline, 12-weeks, and 24-weeks, using structured self-report. Medications were grouped into three categories: Central Nervous System (CNS), Antiretroviral (ARV), and Other. Participants completed the Beck Depression Inventory-II and a symptom inventory developed for this study to assess HCV treatment side-effect severity.

**Results:** Mixed effects analyses showed no significant Time effects for adherence for any of the medication categories for those who completed 24 weeks of treatment (CNS [Z = -0.70568, p = 0.48039]; ARV [Z = 1.10665, p = 0.26845]; Other [Z = 0.32323, p = 0.74652]). Correlational analyses comparing change from Baseline to 12 weeks revealed significant relationships between (1) change in CNS adherence score with (a) change in depression (r = -0.512; p = 0.018) and (b) change in treatment side-effects (r = -0.510; p = 0.018); and (2) change in Other adherence score and change in treatment side-effects (r = -0.363; p = 0.023). Of the 56 participants, 42.9% added growth factors and 14.3% added CNS medications to their existing regimen to manage treatment side effects during treatment.

**Conclusions:** We found no significant decrease in overall medication adherence in patients initiating HCV treatment. We did find a relationship between 12-week adherence decreases in CNS and Other medications and increases in symptoms in the context of HCV treatment.



## 70644 Can Non-Injecting Drug Use Protect against Blood-Borne Viruses among People who Inject Drugs? Evidence from Tallinn, Estonia, and New York City, USA

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**Objectives:** Many injecting drug users (IDUs) also use drugs through means other than injecting (e.g., smoking, snorting, oral). If the non-injecting use substitutes for injecting use, then non-injecting use might protect against infection with blood-borne viruses (BBVs).

**Methods:** In New York City (NYC), 726 IDUs were recruited at a short-term drug detoxification program from 2005-2010. In Tallinn, respondent driven sampling was used to recruit 350 IDUs for a cross-sectional survey in 2007. In both sites, a structured interview was administered and serum samples were collected. Four focus groups were conducted in Tallinn to explore reasons for non-injecting use.

**Results:** In New York, HCV prevalence was 71% among 726 subjects. In a multiple logistic regression analysis, HCV seropositivity was negatively associated with recent intranasal use of heroin (AOR = 0.52, 95% CI 0.33-0.82) and recent intranasal use of speedball (AOR = 0.41, 95% CI 0.21-0.80). HIV prevalence was 16% and associated with sexual risk but not injecting risk. In Tallinn, HIV prevalence was 59% among 350 subjects. In multivariate analysis, recent non-injecting use of drugs other than alcohol was negatively associated with HIV seropositivity (AOR 0.49; 95%CI 0.25-0.97). HCV testing was not conducted. Focus group members specifically mentioned non-injecting use when clean injection equipment was not available.

**Conclusions:** In two different epidemiologic situations, self-reported non-injecting drug use was strongly associated with a lower probability of infection with a BBV. Encouraging intranasal use as an alternative to injection among current IDUs may be a viable strategy for reducing transmission of BBVs.

## 70688 Expression of Heat Shock Protein 27 and Caspase-3 in Hepatitis C Virus-Related Hepatocellular Carcinoma: Relation to Tumor Progression

Hoda A El Aggan (presenting), Abeer Ibrahim, Nevine El Deeb, Ahmed Zeid

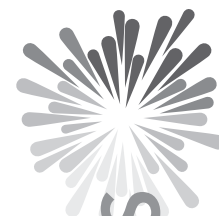
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**Background:** Hepatitis C virus (HCV) is a major risk factor for development of hepatocellular carcinoma (HCC), however, the mechanism of hepatocarcinogenesis in HCV infection is still undefined. Heat shock protein (HSP) 27 is a chaperone molecule with potent anti-apoptotic properties through inhibition of caspase-3 activation and may play a role in carcinogenesis. Therefore, the aim of the present work was to study the expression of HSP27 and caspase-3 in patients with HCV-related HCC in relation to tumor progression.

**Methods:** Twenty cirrhotic patients with HCV-related HCC were enrolled in the study. The severity of liver disease was assessed according to the Model for End Stage Liver Disease (MELD) score. The tumor stage was classified using the scoring system proposed by the Cancer of the Liver Italian Program (CLIP). Histological grading of tumors was performed according to the Edmondson and Steiner's criteria and the surrounding liver tissue was examined for the presence of cirrhosis and steatosis. Expression of HSP27 and caspase-3 was studied in HCC and adjacent non-neoplastic liver tissues by immunohistochemistry. The staining intensity of the tumor was designated as "negative/low expression" when the stained cells were  $\leq 25\%$  of the total and as "high expression" if  $> 25\%$  of cells were positively-stained.

**Results:** HCV-related HCCs showed a significant increase in HSP27 expression and a significant decrease in caspase-3 expression as compared with adjacent non-neoplastic liver tissues ( $P = 0.029$  and  $P = 0.040$ , respectively). The expression of HSP27 showed an inverse correlation with caspase-3 expression in HCC tissues ( $r = -0.691$ ,  $P = 0.001$ ). High HSP27 expression and negative/low caspase-3 expression in HCCs were associated with significant increases in serum levels of aminotransferases, HCV RNA and alpha-fetoprotein, MELD score, tumor size, tumor stage, histological tumor grade, body mass index and the presence of steatosis in the surrounding liver tissue ( $P < 0.05$ ). No relationship was found between expression of HSP27 and caspase-3 in HCCs and age, gender, apparent duration of HCV infection, and tumor encapsulation, multiplicity, location and lymphocyte infiltration ( $P > 0.05$ ).

**Conclusion:** HSP27 plays an important role in the pathogenesis and progression of HCC in HCV infection through inhibition of caspase-3 mediated cell apoptosis and may serve as a potentially useful therapeutic target.



## 70689 MAGE-1 and MAGE-3 mRNA Expressions as Molecular Biomarkers in Patients with Hepatitis C Virus-related Hepatocellular Carcinoma.

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**Background:** The melanoma antigen (MAGE) family members are tumor-specific antigens exclusively expressed in neoplastic cells and may relate to the pathogenic mechanism of tumors and cancer diagnosis. Therefore, the present work was designed to study the expression of MAGE-1 and MAGE-3 mRNAs in the peripheral blood and cancerous tissues of patients with hepatitis C virus (HCV)-related hepatocellular carcinoma (HCC).

**Methods:** Thirty patients with HCV-related cirrhosis (15 patients with HCC and 15 patients without HCC) and 15 healthy subjects were enrolled in the present study. The severity of liver disease was assessed according to Child-Pugh scoring system. The HCC clinical stage was classified using the scoring system proposed by the Cancer of the Liver Italian Program (CLIP). Histological grading of HCC was performed according to the Edmondson and Steiner's criteria. Expression of MAGE-1 and MAGE-3 mRNAs in peripheral blood samples, HCC specimens and surrounding non-neoplastic liver tissues, were studied by a reverse-transcription polymerase chain reaction (RT-PCR) with the specific primers after RNA extraction. The sensitivity and specificity of MAGE-1 and MAGE-3 mRNAs as markers for diagnosis of HCC have been assessed by plotting a receiver-operating characteristic (ROC) curve.

**Results:** In HCC patients, the positive rate of MAGE-1 and MAGE-3 mRNA expression was 53.3% and 33.3% in peripheral blood samples respectively, whilst the positive rate was 53.3% and 40.0% in HCC tissue samples, respectively. By contrast, MAGE-1 and MAGE-3 mRNA were not detected in the adjacent non-neoplastic liver tissues or in the peripheral blood samples of cirrhotic patients without HCC and healthy subjects. No relationship was found between MAGE-1 and MAGE-3 mRNA expression and age, gender, Child-Pugh score, tumor size, clinical stage and histopathological grade ( $P > 0.05$ ). The sensitivity and specificity of MAGE-1 mRNA as a marker for the diagnosis of HCC was 53.3% and 100%, respectively, while MAGE-3 mRNA has a sensitivity of 40% and a specificity of 100%.

**Conclusions:** MAGE-1 and MAGE-3 mRNA are highly expressed in HCV-related HCCs and may play a role in hepatocarcinogenesis. These tumor-specific antigens can be used as molecular markers for early diagnosis of HCC and detection of disseminated tumor cells and may act as a potential target for immunotherapy in HCC patients.

## 70752 A Novel Approach for a New Era: Successful Integration of Multidisciplinary, Hepatitis C Care within an Established HIV Primary Care Practice

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**Background:** Clinical trials have shown that at least 40% of patients with chronic hepatitis C (HCV) achieve sustained virologic response (SVR) with peginterferon/ribavirin (Peg/RBV). Since patients with a history of mental illness, addiction, multiple medical comorbidities or unstable social situations are commonly excluded from research trials, SVR is achieved less often in clinical practice. These issues may present management dilemmas for clinicians unaccustomed to the needs of complex patients. We proposed that integration of an HCV treatment program into an existing multidisciplinary HIV primary care practice would better address these needs, resulting in improved treatment outcomes.

**Methods:** An internist-led HCV treatment program was integrated into an existing HIV practice employing a successful chronic care model, akin to a patient-centered medical home. Principle staff included a general internist with experience in viral hepatitis management, a licensed social worker (LSW), registered-nurse/case manager (RN) and dietician. Intensive patient education and adherence support was provided by the RN and LSW, focusing on psychosocial issues, coordination of mental health services and resolving barriers to care. Emphasis was placed on stabilization of modifiable psychiatric and medical comorbidities to allow for initiation of Peg/RBV in patients who would not normally receive treatment. Treatment outcomes were continually monitored.

**Results:** 76 patients initiated Peg/RBV. None were coinfecting with HIV. Genotype (GT) 1 HCV predominated (72%), followed by GT 2 (14%), GT 3 (9%) and other GT (4%). 71% completed therapy. Adverse events (AEs) were typical of Peg/RBV. Medical AEs were the most common reason for discontinuation (31%); only 2 patients discontinued for psychiatric reasons. Of 61 patients with final outcome data, SVR was achieved in 57% (35), GT 1 (51%, 23), GT 2 (86%, 6), GT 3 (67%, 4) and other GT (67%, 3). 15 patients remain on Peg/RBV.

**Conclusions:** Integration of HCV and HIV treatment services resulted in high rates of therapy completion and SVR. Focusing efforts on education, adherence support, health stabilization and patient preparedness for treatment allowed Peg/RBV to be provided to a broader population. Further evaluation of this model of care is necessary in HIV treatment centers and other patient-centered medical homes, where medical, case management, mental health, and nutrition services may be co-located.



## 70762 Directly Observed HCV Treatment in Methadone Clinics – Preliminary Results

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**Background:** Most methadone-maintained injection drug users (IDUs) have been infected with hepatitis C virus (HCV), but few initiate HCV treatment. Physicians may be reluctant to treat HCV in IDUs because of concerns about treatment adherence, psychiatric comorbidity, or ongoing drug use. Optimal HCV management approaches for IDUs remain unknown.

**Objective:** We sought to determine whether modified directly observed therapy (mDOT), compared to treatment as usual (TAU), improves adherence and virologic outcomes among methadone-maintained opioid users.

**Methods:** We conducted a randomized controlled trial in a network of nine methadone clinics with onsite HCV care located in the Bronx, New York. We enrolled HCV-infected adults initiating care with pegylated interferon alfa-2a (IFN) plus ribavirin, and randomized them to mDOT (directly observed daily ribavirin plus provider-administered weekly IFN) or TAU (self-administered ribavirin plus provider-administered weekly IFN). Our outcome measures are: 1) self-reported and pill count adherence to ribavirin at 12 and 24 weeks, and 2) proportion of subjects with end of treatment response (ETR), or sustained viral response (SVR). We used mixed effects linear models to assess differences in pill count adherence between treatment arms (mDOT v. TAU), and assessed differences in ETR and SVR between treatment arms with chi square tests.

**Results:** 58 subjects have enrolled to date. Of the first 40 subjects enrolled: 21 were randomized to mDOT and 19 to TAU. The sample is 77% Latino, 38% active drug users, and 27% HIV-infected. We observed significant differences in pill count adherence between treatment arms at both 12 weeks (88% in mDOT arm vs. 81% in TAU arm,  $p = 0.04$ ) and at 24 weeks (88% in mDOT arm vs. 77% in TAU arm,  $p = 0.02$ ). We did not observe difference in adherence to IFN between treatment arms (96% in mDOT arm vs. 94% in TAU arm). Most (81%) subjects in mDOT arm achieved >80% adherence, vs. only 53% in TAU arm ( $p = 0.09$ ). We did not observe differences in virological outcomes between treatment arms: 67% ETR and 44% SVR in mDOT arm vs. 61% ETR and 40% SVR in TAU arm.

**Conclusion:** Among methadone-maintained, HCV-infected adults, directly observed ribavirin administered at methadone clinics is associated with increased adherence to ribavirin, compared to treatment as usual. Early results show no differences in virologic outcomes between treatment arms, likely because all subjects received provider-administered IFN.

## 70764 Shift in Th1/Th2 Cytokine Patterns in Hepatitis B Virus-Positive Patients Coinfected with HIV

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**Background:** Antiretroviral drugs have immensely improved the standard of life of HIV-positive patients, maximally reducing the occurrences of most opportunistic infections. However due to similarities in mode of transmission more HIV patients are also being infected with hepatitis B virus (HBV), resulting in increase in morbidity and mortality rates, mostly from lung diseases. Th1 cytokines have been shown to positively correlate with hepatic inflammation and they are secreted at higher levels than Th2 cytokines in chronic HBV infection. The aim of this study was to evaluate Th1/Th2 cytokine profiles of HBV/HIV-coinfected patients.

**Methods:** Serum of 50 controls and 5 HBV/HIV co-infected patients were analysed and HIV-1 viral load measured using the Abbott Real-Time HIV-1 assay (Abbott Molecular Inc., Des Plaines, IL), CD4 T cell counts using the BD FACSCanto II flow cytometer (Beckton Dickinson, CA) and Th1/Th2 cytokine levels using ELISA (MABTECH AB, Sweden). Cytokines evaluated include IL-4, IL-6, IL-10, IL-13, IL-1b, IL-2, IL-17 and TNF-alpha.

**Results:** Th1 cytokines occurred at generally lower levels than Th2 cytokines with IL-17 and TNF-alpha being undetectable in all studied patients, while IL-2 and IL-1b were secreted at moderately high levels with mean value of 72.48 pg/ml and 91.14 pg/ml, respectively. Th2 cytokine IL-10 had the highest level of secretion with mean value 274.3 pg/ml and IL-6, IL-13 and IL-4 also had higher levels of secretion with mean values 240.8 pg/ml, 77.2 pg/ml and 156.4 pg/ml, respectively.

**Conclusions:** Increased Th2 responses with increased Th2 cytokines secretion as observed in this study shows a shift in cytokine patterns from Th1 cytokines in HBV patients to Th2 cytokines in HBV/HIV-coinfected patients. This study also agrees with previous studies which state that Th2 responses may be associated with persistence of HBV infection in HBV/HIV-coinfected patients.



## 70799 Undetectable HCV RNA in Peripheral Blood Mononuclear Cells (PBMC) May Allow Shorter Treatment Duration in HIV/HCV Coinfection

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**Background:** Duration of HCV treatment in HIV/HCV-coinfected individuals remains intolerable to many individuals. Evidence of clearance from sanctuary sites (eg PBMC) may allow shorter duration of treatment.

**Methods:** 5 individuals who were felt would benefit from shortened treatment durations had PBMC HCV RNA measured at the end of treatment. PBMCs were isolated and reconstituted in PBS to 1X10<sup>7</sup> cells/vial. Intracellular HCV RNA was extracted using QIAamp RNA Blood MiniKit (Qiagen). Reverse transcriptase PCR was performed using a modification of the COBAS TaqMan HCV Test for use with the high pure system (Roche Diagnostics). HCV RNA could be detected to at least 600 IU/1X10<sup>7</sup> cells.

**Results:** Three individuals had chronic hepatitis C. One with G3 virus had to discontinue treatment at 24 weeks, despite not achieving a RVR, due to toxicity. The PBMC HCV RNA was undetectable at this time. The other two had low baseline HCV RNA levels, achieved RVR and discontinued treatment at week 12 after an undetectable PBMC HCV RNA. All three went on to achieve SVR. More recently two individuals with G1 hepatitis C diagnosed between 1 and 2 years after acquisition, achieved RVR, had undetectable PBMC HCV RNA at week 20 and discontinued treatment at week 24 with an ETR. SVR are awaited.

**Conclusion:** Demonstration of an undetectable HCV RNA in PBMC at the end of treatment may allow shorter durations of therapy in certain HIV/HCV-coinfected individuals. A controlled trial is required to confirm these findings.

## 70800 Chronic Hepatitis E in HIV as a Cause for Cryptogenic Cirrhosis

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**Background:** Chronic hepatitis E infection is increasingly being reported in immunocompromised patients. We describe a case of chronic hepatitis E cirrhosis in an HIV-positive Caucasian man who demonstrated persistently elevated Alanine Transferase (ALT) levels predating commencement of highly active antiretroviral therapy (HAART).

**Case report:** A 45-year-old HIV-positive captain of a ship was found to have a persistently elevated ALT at 335 IU per liter at the time of HIV diagnosis in January 2000 at our centre (CD4 2 cells/ml, HIV 36,000 viral load copies/ml). He was hepatitis A immune, and had natural immunity to hepatitis B. Polymerase chain reaction (PCR) tests were repeatedly negative for hepatitis C, syphilis, cytomegalovirus and Epstein-Barr virus. Serological tests were negative for autoantibody screens,  $\alpha$ 1-antitrypsin, iron and copper studies. His HIV viral load was fully suppressed since June 2000 on HAART with a rise in CD4 count >200 copies/ml. He was asymptomatic and had no relevant history to suggest a cause for chronic liver disease, including minimal alcohol use and his examination was normal with absence of neurological signs. A liver biopsy in 2006 revealed stage 4 fibrosis with moderate, spotty necrosis. In 2007, an ultrasound elastography assessment revealed progression to cirrhosis with a reading of 69.1kPa. In March 2010, hepatitis E (HEV) IgM and IgG were detected and HEV (genotype 3) infection was confirmed by the detection of HEV RNA in his serum. Testing of stored plasma samples for HEV RNA revealed the patient had been persistently viraemic since March 2000 with relatively unchanged HEV RNA levels at an average of log<sub>5.6</sub> copies/ml over time. He was serologically silent from March 2000 until May 2001. However, plasma samples were positive for both HEV IgM and IgG from October 2001 to date. A trial of pegylated-interferon alpha-2a (Pegasys) was commenced to treat his HEV infection. After 3 weeks of Pegasys, his plasma HEV RNA levels were undetectable and his ALT improved significantly.

**Discussion:** Unexplained liver dysfunction in HIV-positive patients may be attributable to chronic HEV infection. Discrepancies between serological and PCR results shown in this patient demonstrate the importance of considering molecular techniques to exclude HEV infection. It is planned for him to undergo therapy for at least 24 weeks and a progress report will be provided.



## 70806 Chronic Hepatitis C Patient Navigation Case Studies

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**Introduction:** Hepatitis C treatment is difficult, and many patients do not receive treatment. There are multiple barriers that prevent treatment completion. Navigators help individuals transverse the healthcare system, removing barriers. Studies of cancer care navigation have demonstrated that patients value navigators as a source of emotional, educational, and practical support. Navigators form close, supportive relationships that help to identify and address issues that can cause treatment interruption and/or cessation.

**Description:** Three cases of successful navigation in an urban Primary Care HCV Clinic setting serving a largely minority population will be presented: 1) Navigator arranged for psychiatric consult and medical leave for patient who developed neuropsychiatric side effects on treatment; 2) Navigator arranged for enrollment in patient assistance program for patient whose benefits reached the maximum cap during treatment; and 3) Navigator assisted a patient who lost Medicaid mid-treatment by escorting the patient to entitlement appointments, arranging for uninterrupted care through pharmaceutical assistance and hospital sliding scale medical coverage.

**Lessons Learned:** Navigators serve as an important link between patient and medical staff to facilitate appropriate and timely referrals. Successful navigation requires: 1) Understanding of HCV treatment; 2) Detailed knowledge of relevant entitlements, insurance plans, and assistance programs; and 3) Interpersonal skills needed to help patients tolerate the frustration of barriers. Successful navigators must be flexible, persistent, creative, culturally sensitive, and invested in advocating for patients.

**Recommendations:** Navigators need training in HCV treatment protocol, entitlements, health insurance policies, patient assistance programs, and interpersonal skills. HCV treatment navigators must be well integrated into the treatment team by participating in all staff meetings and case conferences. Alternate funding must be identified due to non-billable navigator services through state and federal health coverage programs. Further study demonstrating the effectiveness of navigation in HCV treatment retention is warranted.

## 70851 Interferon-Gamma versus Amantadine in Combination with Interferon-Alfa-2b and Ribavirin in Chronic Hepatitis C Genotype 3 Non-Responders and Relapsers

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**Background:** The aim of the present study was to evaluate the efficacy and safety of triple-combination regimens comprising of interferon alfa-2b and ribavirin plus either interferon-gamma or amantadine in HCV genotype 3-infected patients who have not previously responded or relapsed to interferon-alfa in combination of ribavirin.

**Methods:** Patients were randomized to receive interferon alfa-2b 3MU thrice a week, ribavirin 800-1200 mg per day with either interferon-gamma 2 MU thrice a week or amantadine 100 mg twice daily. Treatment was continued for 48 weeks in patients showing complete or partial (2 log reduction) early virological response (EVR) at 12 weeks and negative PCR at 24 weeks.

**Results:** Total enrollments were 44. Mean age 44.1 years (28-60); 25 were previously non-responders out of them 12 were in the gamma arm. Nineteen were relapsers, out of them 10 received interferon-gamma. F3 or F4 fibrosis was seen in 14 (34%) and 9 (23%) were diabetic. By intention-to-treat analysis, the overall early virological response (EVR) with triple regimens was 61.4% (27/44). The EVR for interferon-gamma arm was 72.7% (16/22) and for amantadine arm 50% (11/22) ( $p = 0.089$ ). The overall end of treatment response (ETR) was 40.9% (18/44). The ETR was 50% (11/22) and 31.8% (7/22) for interferon-gamma and amantadine arms, respectively ( $p = 0.220$ ). The overall sustained virological response (SVR) was 38.6% (17/44). SVR was 50% (11/22) in the gamma arm and 27.27% (6/22) in the amantadine arm ( $p = 0.122$ ). In the subgroup analysis, this figure was 60% (6/10) and 44% (5/9) for relapsers ( $p = 0.845$ ), and 41.6% (5/12) and 7.69% (1/13) for non-responders ( $p = 0.047$ ) in the gamma and amantadine arms, respectively. Treatment was well tolerated in both arms.

**Conclusions:** About one third of genotype 3 patients who had not previously responded well to the interferon-alfa and ribavirin responded to the triple regimens. However addition of interferon-gamma showed to be a much better option with an acceptable safety profile. Half of the patients who did not respond to or relapse to previous treatment by interferon-alfa plus ribavirin showed SVR by this triple therapy of gamma interferon-gamma plus interferon-alfa plus ribavirin; its combination with pegylated-interferon and ribavirin needs further evaluation in a larger clinical trial.



## 70970 Quantitation of ITX 5061, a Scavenger Receptor Class B, type I Antagonist in Human Plasma with LCMS

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**Background:** ITX 5061 is a highly potent small molecule inhibitor of scavenger receptor class B, type I, an integral transmembrane protein that is found in liver cells and has been found to be actively involved in the transport of hepatitis C virus into hepatocytes. To determine the pharmacokinetics of ITX 5061, a method for the quantitation of this pharmaceutical compound in human plasma was required. Mass spectrometry interfaced with liquid chromatography is the state of the art for bioanalysis of small molecules and was evaluated for this assay.

**Methods:** An ITX 5061 assay was validated using 2001 FDA guidance for bioanalytical methods. A standard curve with low, medium and high quality controls was prepared in human plasma. An analog of ITX 5061 was employed as internal standard. After protein precipitation, compounds were separated by isocratic reverse phase chromatography and detected via electrospray ionization mass spectrometry. Multiple reaction monitoring in positive mode was employed with ITX 5061 monitored at 585/114, and the IS at 592/122. Stability, matrix effect, precision and accuracy were measured.

**Results:** The quantitation range of 2.5 to 5000ng/mL was linear and was weighted (1/x<sup>2</sup>). At the lower limit of quantitation, intraassay precision ranged 8 to 13% over 6 assays and the interassay was 13%. The intraassay precision of low, medium and high controls ranged 2-6%, 1-4%, and 0-2%, respectively; interassay precision was 4%, 2%, 1%, respectively. Accuracy was acceptable for each analysis ( $\pm 15\%$ ). Samples may be kept at room temperature for 5.5 hours, thawed three times, and diluted 10-fold. The method was free from matrix effects, including hemolyzed or lipemic plasma.

**Conclusions:** A chromatographic method using tandem mass spectrometry for detection of ITX 5061 concentrations has been validated and may be utilized to determine the human pharmacokinetics of ITX 5061.

## 70980 HCV Treatment in HIV-Coinfected Patients with Renal Disease

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**Background:** HCV/HIV-coinfected patients are difficult to treat and SVR rates are low. Renal disease represents an additional therapeutic challenge. There is scant information on HCV treatment in patients with HCV, HIV and chronic kidney disease (CKD). We report here our experience in tertiary academic center Methods. In this retrospective and longitudinal study we identified all patients with HIV/HCV coinfection and CKD treated for HCV with pegylated-interferon and ribavirin between 2000 and 2010 in our center. CKD was defined and staged according to NKF Classification.

**Results:** Seven patients, 5 male, majority black (6/7), with a median age of 54 years were identified. Median METAVIR liver fibrosis score was F2, HCV genotype was 1 in 6/7 and most patients had high HCV RNA. Their median CD4 count and CKD stage were 480 cells/mm<sup>3</sup> and 4 and, respectively. Median treatment duration was 14 weeks. HCV therapy was not discontinued due to side effects in any case. Median ribavirin dose was 200 mg/day at treatment initiation and was decreased throughout treatment in 4 patients, often on a monthly basis. Pegylated-interferon was dosed according to kidney function. The median drop in hemoglobin levels during treatment was 5.1 g/dL (range 3-5.6). Virological failure occurred in 5/7 patients, with only two patients responding and completing the planned 48 weeks.

**Conclusions:** The challenges for HCV treatment posed by patients living with HIV, HCV and CKD explain the small sample of our study. While changes in ribavirin doses were frequent, there were not treatment discontinuations due to side effects, suggesting that larger investigations are possible from a toxicity standpoint. Nevertheless, SVR rates were low and direct-acting antivirals should be studied in this special group of patients to increase the treatment success rate.



## 70989 Validation of Serum Biomarkers for the Prediction of Significant Liver Fibrosis Using Transient Elastography in HIV-Infected Patients with Nonalcoholic Fatty Liver Disease with and without Chronic Hepatitis C

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**Background:** Liver damage due to nonalcoholic fatty liver disease (NAFLD) is currently one of the leading causes of hypertransaminasemia and liver fibrosis (LF) progression in HIV-infected patients on antiretroviral therapy. Transient elastography (TE) has been well validated for staging liver fibrosis in patients with chronic viral hepatitis, including those coinfecting with HIV. Preliminary data supports good performance of TE for assessing liver fibrosis in patients with NAFLD in distinct populations. The accuracy of serum biomarkers for staging LF in HIV-infected patients with NAFLD has not been examined.

**Methods:** All HIV-monoinfected and HIV/HCV-coinfecting patients with severe hepatic steatosis (HS) followed at a reference HIV clinic in Madrid were included in a prospective study. Severe HS was diagnosed by abdominal ultrasound, which generally only recognize >30% fatty hepatocytes, by a single trained operator. Patients with HBV coinfection, alcohol abuse and/or autoimmune or metabolic disorders were excluded from the study. Significant and advanced LF was defined in the presence of liver stiffness values above 7.8 and 9.5 kPa, respectively. NAFLD, BARD, APRI and FIB-4 indexes were calculated in parallel.

**Results:** A total of 322 patients were included in the study, 71% (n = 230) HIV-monoinfected (median age 49 years, 88% males, 9% IDUs, median BMI 25 kg/m<sup>2</sup>) and 29% (n = 92) HIV/HCV-coinfecting (median age 47 years, 78% males, 81% IDUs, median BMI 24 kg/m<sup>2</sup>). Taking as reference TE categorization of liver fibrosis in HIV-monoinfected patients, PPV and NPV for significant liver fibrosis were as follows: 30.1% and 89.6% for NAFLD score; 20% and 81.7% for BARD; 34.3% and 81.1% for APRI; and 25% and 82.1% for FIB-4, respectively. These figures for advanced liver fibrosis were as follows: 66.7% and 91.3% for NAFLD score; 10.5% and 88.2% for BARD; 40% and 89% for APRI; and 50% and 88.4% for FIB-4 scores. When comparing HIV-monoinfected vs HIV/HCV-coinfecting patients, NAFLD score showed the highest NPV for assessing significant liver fibrosis (89.6% vs 62.5%; p = 0.003) and advanced liver fibrosis (91.3 vs 58.2%; p = 0.001).

**Conclusions:** All BARD, NAFLD, APRI and FIB4 scores are helpful to exclude significant and/or advanced liver fibrosis in HIV-monoinfected patients with NAFLD. Thus, they may be helpful for avoiding liver biopsy when TE is not definite (stiffness values between 7.9 and 9.5 kPa). Even if NAFLD score shows the best accuracy in HIV-monoinfected patients, it underperforms in HIV/HCV-coinfecting subjects.

## 71156 Therapeutic Drug Monitoring (TDM): Application for Assessing Drug Interactions in HIV/HCV-Coinfected Patients

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**Background:** The development of numerous new STAT-C agents, potential for metabolic induction or inhibition, will require that innovative study designs be developed to assess drug interactions in HIV-infected patients receiving combination antiretrovirals (cARV). In a recent TDM study of 275 HIV-infected patients, we utilized directly observed dosing and TDM in a subset of HIV/HCV-coinfecting individuals (n = 94) and evaluated atazanavir (ATV) (n = 67) and lopinavir (LPV) (n = 48) trough plasma concentrations. The objective of this analysis was to identify patients at the upper and lower end of the therapeutic range for inclusion/exclusion in HCV antiviral drug interaction studies.

**Methods:** For TDM, individuals were on ATV (300 mg and 100 mg ritonavir [RTV] daily) or LPV (400 mg and 100 mg RTV twice daily)-containing regimens. Trough plasma concentrations (22-26 hours for ATV and 10-14 hours for LPV) were measured using HPLC. HCV status was evaluated by serology.

**Results:** Considerable interindividual variability of ATV and LPV was noted [HCV vs. non-HCV, median (range), ATV: 0.439 (0.050-1.382) vs. 0.678 (0.050-1.567), LPV: 5.079 (0.100-7.880) vs. 5.680 (2.450-8.004)]. Significantly lower median LPV trough concentrations were noted among patients with HCV during TDM evaluated as an independent variable (2.253 vs. 5.927 mcg/mL, P = 0.032). HCV was not associated with ATV trough concentrations.

**Conclusions:** During TDM, wide interindividual variability of ATV and LPV trough concentrations was observed, with significant associations noted for HCV and lower LPV trough concentrations. These data suggest that TDM for cARV identifies patients who may or may not be good candidates for the addition of new STAT-C agents based on metabolic induction versus inhibition characteristics. In addition, TDM would provide a mechanism for continued monitoring during drug interaction studies.



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INTERNATIONAL CONFERENCE ON  
VIRAL HEPATITIS

April 11-12, 2011

To Whom It May Concern:

This letter is a confirmation that \_\_\_\_\_ attended the International Conference on Viral Hepatitis, held April 11-12, 2011, at the Grand Historic Venue & Tremont Plaza Hotel in Baltimore, MD, United States. This 1.5-day conference was jointly sponsored by the International Association of Physicians in AIDS Care (IAPAC); University of Bonn, Germany; and Johns Hopkins University.

Sincerely,

José M. Zuniga, PhD, MPH  
President/CEO, IAPAC





# VIRAL HEPATITIS 2011: POLICY AND PUBLIC HEALTH

Official Satellite Symposium of the  
*International Conference on Viral Hepatitis*



1:30 P.M. – 3:30 P.M., Tuesday, April 12, 2011  
Grand Historic Venue – Corinthian Room

Given recent events in national public policy that may impact people at-risk and/or living with chronic hepatitis B and C in the United States, the medical workforce must not only have the clinical tools but all the public health tools necessary to fully prevent, treat, and care for those affected.

This symposium will include a panel of presenters representing different stakeholders in the viral hepatitis movement including a national advocate, public health professional, medical provider, and federal government partner.

## LEARNING OBJECTIVES

At the conclusion of this symposium, participants will be able to:

- Describe the current US federal response to the viral hepatitis epidemics and the challenges of those seeking services;
- Understand the viral hepatitis public health landscape including current recommendations by key federal agencies for medical professionals and providers including the Institute of Medicine Report on Viral Hepatitis, the HHS Viral Hepatitis Action Plan and health reform;
- Describe the viral hepatitis national advocacy movement including ability to identify key Congressional players and opportunities to participate in local, state and national viral hepatitis advocacy activities; and
- Identify public health strategies to engage with local and state health departments, specifically the Adult Viral Hepatitis Prevention Coordinators, and other health professionals to expand and/or improve upon current medical practices.

## SYMPOSIUM PROGRAM

### **From Bench to Clinic: Translating Research Advances into Clinical Practice**

Mark S Sulkowski, MD • Johns Hopkins School of Medicine, Baltimore, MD

### **Are Advocates, Clinicians and Policymakers Ready?**

Chris Taylor • National Alliance of State & Territorial AIDS Directors (NASTAD), Washington, DC

### **HRSA HAB Viral Hepatitis Activities Update**

Adan Cájina, MS • Health Resources and Services Administration (HRSA), Rockville, MD

### **The Role of Public Health in the Viral Hepatitis Movement**

Yasir Shah • DC Department of Health, Washington, DC

### **National Policy and Opportunities for Viral Hepatitis**

Colin Schwartz • National Alliance of State & Territorial AIDS Directors (NASTAD), Washington, DC

NASTAD strengthens state and territory-based leadership, expertise, and advocacy and brings them to bear in reducing the incidence of HIV and viral hepatitis infections and on providing care and support to all who live with HIV/AIDS and viral hepatitis. NASTAD's vision is a world free of HIV/AIDS and viral hepatitis.

IAPAC's mission is to improve the quality of HIV, hepatitis, malaria, and tuberculosis prevention, care, and treatment services worldwide. IAPAC represents more than 17,000 physicians and allied health professionals in over 100 countries.



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