Detecting and Evaluating Drug-Induced Liver Injury and Dysfunction

What’s Normal? What’s Not? What Should We Do About It?

DILI remains a major problem for drug development, and a clinical concern after marketing. We need new understanding, better communication, to avoid the problems. This academic-industry-government international conference will discuss new findings and thinking about drug-induced liver injury (DILI) and dysfunction (DILD), with presentations by experts in clinical hepatology and other fields, and active discussion with all registrants. Come and participate in this conference.

Organizers: John R. Senior and Lana Pauls, with advice from Mark Avigan, Michael Merz, Arie Regev, Leonard Seeff, Paul Watkins

Inn and Conference Center, University of Maryland, 20-21 March 2013
3501 University Boulevard, East Hyattsville MD 20783

Wednesday, 20 March 2013

7:30 Continental Breakfast outside the conference room
8:00 Introductions and Opening Statements
   Genesis of the DILI Conferences 1999-2013 (5’)
   Introduction of the Chinese Delegation (5’)
   Developing Consensus-Driven Standards for Understanding DILI (20’)

8:30 Session I: What are “normal” liver test results?
   Moderators: Paul Watkins and Leonard Seeff

   8:30 How much and what testing assures normality?
   John Senior, CDER/FDA

   8:45 What is a “normal” value for serum ALT activity?
   D. Robert Dufour, VAMC

   9:00 Cut-off values for interrupting or permanently stopping new drugs -
   Arie Regev, Lilly

   9:15 Use xB versus xULN for assessing drug effects?.
   Leonard Seeff, Hill Group

   9:30 Open discussion

   Break

   Session IB: How should we make decisions in clinical trials?

   10:15 Balancing the risks of harms and chances of benefits
   Christine Hunt, Duke U

   10:35 Understanding each other across disciplines, organizations
   Doug Throckmorton, FDA

   11:00 Misunderstandings, Misnomers, Miscommunications,
   Lana Pauls, FDA

   11:15 General discussion – panel of speakers above, audience
   Panel; Audience

   12:00 Lunch

   Session IIA: The Coming Crush: Is There a Cure Out There for Hepatitis C?
   Moderators: Christine Hunt and John Senior

   1:00 A coming flood of new drug applications for treating hepatitis C
   Debra Birnkrant, FDA

   1:20 Hepatitis C: End of the beginning or beginning of the end?
   Harvey Alter, NIH

   1:40 Predicting trial outcomes using baseline and on-study data
   Marc Ghany, NIH

   2:00 How to rule out DILI in subjects with active liver disease
   Leonard Seeff, FDA/SGE

   2:15 General discussion – panel of speakers above, audience
   Panel; Audience

   2:55 Break

   Session IIB: How can we manage it?

   3:15 Antiviral management information system
   Jeff Florian, CDER/FDA

   3:30 A view from the medical regulatory side
   Ed Cox, CDER/FDA

   3:45 A view from the industry side
   Gary Davis, Baylor

   4:00 A view from academia (AASLD)
   T. Jake Liang, NIH

   4:15 General discussion – speakers and audience
   All

   4:45 --- Reception: wine and cheese, mingle and relax ---

   5:30 Dinner on your own, but maybe not too far away, so you may join the evening debate

   Session IIIC: Does the July 2009 Guidance on Drug-Induced Liver Injury Need Updating, Revision?
   Moderators: Arie Regev, Robert Temple, and Ruyi He

   7 – 9 Further discussion of needs for revision, clarification of FDA guidance July 2009

   Main meeting room
Thursday, 21 March 2013

Continental Breakfast outside the conference room

8:00

Session III: Everybody says we need new biomarkers; are there any good ones?
Moderators: Mark Avigan and Michael Merz

Session IIIA: New biomarkers for DILI
8:00 Should be better than {ALT & BILI} together
John Senior, FDA
8:15 Pre-marketing ALT predicts post-marketing liver safety
Cynthia Moylan, Duke U
8:30 Serum miRNA markers for human DILI
Shashi Bala, U MA
8:45 Possible mechanisms of lapatinib hepatotoxicity
Christopher MacLauchlin, GSK
9:00 General discussion – speakers and audience
All
9:30 Break

Session IIIB: Interdependence of organ functions
10:00 Drug-induced hepatic encephalopathy
Will Lee, UTSW
10:15 Kidney-liver dependency – lessons from the hepatorenal syndrome
Nancy Xu, FDA/DCRP
10:30 Cardiac hepatopathy
Willis Maddrey, UTSW
10:45 Should oncology patients be evaluated differently for DILI?
Gideon Blumenthal, NIH/FDA
11:00 General discussion – speakers and audience
Panel; All
11:30 Lunch

Session IV: Maximizing what we can learn from clinical development programs
Moderators: Arie Regev and Lana Pauls

Session IVA: Something old; something new; something better
12:30 Can we harmonize across clinical trials to find predictive biomarkers?
Mark Avigan, CDER/FDA
12:45 Getting the right information to assess DILI causality likelihood
Ling Chin, GDU Consulting
1:00 Clarifying classification of liver injury in administrative data
Vincent Lo Re, U Penn
1:15 Proposed Best Practices – from the 9 November conference
Michael Merz, Novartis
1:30 General discussion – speakers and audience
All
2:00 Break

Session IVB: Putting the data together
2:30 The ECG Warehouse/Cardiac Safety Research Consortium
Norman Stockbridge, FDA
2:45 Proposals for eDISH2 development
Ted Guo, FDA/OTS
3:00 Alternative analytical systems for assessing liver safety: interactive graphics
Michael Merz, Novartis
3:30 JReview/JANUS
Chuck Cooper, FDA
3:45 Proposal for a Liver Safety Research Consortium
Paul Watkins, U NC
4:00 General discussion – panel of speakers above, audience
Panel; All
4:30 Adjourn

The program is co-sponsored by the Food and Drug Administration/Center for Drug Evaluation and Research (FDA/CDER), Critical Path Institute (C-Path), and the Pharmaceutical Research and Manufacturers of America (PhRMA).
The program is endorsed by the National Institutes of Health (NIH) drug-induced liver injury network (DILIN), and the American Association for the Study of Liver Disease (AASLD).

Copies of slides shown, and transcripts of speakers’ comments and discussions will be posted on the internet a few weeks after the conference.

For previous programs go to the following websites:
www.fda.gov (type liver toxicity into search window, click on first entry, and page down)
or to www.aasld.org  Training/Education, Drug-Induced Liver Injury 2012 Program

Registration by Critical Path Institute: $600 for industry; $300 for government or academia
Make lodging reservations on your own at the University of Maryland Conference Center
(click on Conference Services, then ; Events/Guests/Registration, then “Book Online”)
Use the special link below to reserve at the reduced lodging rate, $179/night: