Asymmetry of Drug Safety and Efficacy in Clinical Trials with DILI- Toward Quantitative Estimate of Net Benefit to Patients

Paul Watkins, Mark Avigan, John-Michael Sauer, Arie Regev, Gyongyi Szabo, John Senior

Drug-induced liver injury (DILI) is a major problem for drug development and clinical care. Several unresolved problems require new understanding and consensus. Especially difficult is much greater costs (time and money) of adequate safety studies than for the proof of efficacy. This international academic-industry-government conference will discuss current findings and thinking on DILI and drug safety by expert hepatology, toxicology and special presentations. We encourage you to register, come, participate, and debate the issues for development of new agreements and guidance.

Tuesday, 6 June 2017

7:30 continental breakfast outside the conference room; register
8:00 OPENING REMARKS Sweet and Sour DILI Keynotes John Senior

SESSION I Best Practices in Clinical Drug Development
Moderators: Arie Regev and Naga Chalasani

8:05 Special recognition of Neil Kaplowitz' book Yimin Mao
8:10 Alcoholic hepatitis as a drug-induced disorder Gyongyi Szabo
8:30 Detection and management of DILI in NASH/NAFLD subjects in drug development Naga Chalasani
9:50 Reactivation of hepatitis B in clinical trials with immune suppressive drugs Rajender Reddy
9:10 General discussion of issues ALL PRESENT
9:40 mid-morning coffee break
10:00 Chronic liver disease after acute hepatocellular DILI Bob Fontana
10:20 Is chronic liver disease after acute hepatocellular DILI over-estimated? Einar Bjornsson
10:40 Detection and evaluation of DILI in patients with active or advanced liver diseases Jim Lewis
11:00 General discussion of issues ALL PRESENT
11:30 lunch break

12:30 SESSION II Evaluating DILI Signals in Clinical Trials to Inform Benefits, Risks
Moderators: Michael Aleo and Mark Avigan

12:30 How clinical signature of DILI impacts benefits and risks Mark Avigan
12:50 Do pharmacokinetic and hepatocellular steps inform risk assessment? Raj Madabushi
1:10 Current industry perspectives on hepatotoxicity in drug discovery Will Proctor
1:30 Do histologic features inform DILI mechanisms? Dave Kleiner
1:50 Agents that alter immune tolerance; what can we predict? Amy Rosenberg
2:10 General discussion of issues ALL PRESENT
2:40 refreshment break
3:10 Quantitative benefit-risk assessment of DILI Rebecca Noel
3:30 Agents that inhibit the BSEP and mitochondrial function – what do we know? Michael Aleo
3:50 Improved survival—what tradeoffs make sense? Dan Suzman
4:10 Need for consideration of issues for guidance revision Bob Temple
4:30 General discussion of Issues ALL PRESENT

5:00 reception: wine and hors d’oeurves; mingle, chat, and relax --- dinner on your own
Wednesday, 7 June 2017

7:30  continental breakfast outside the conference room

8:00 SESSION III  New Tools for Detection and Assessment of DILI
Moderators: John-Michael Sauer and Neil Kaplowitz

8:00  miRNAs as biomarkers for DILI and as predictors in clinical trials  Herb Bonkovsky
8:20  New methods to predict DILI risk  Jack Uetrecht
8:40  NCTR rule-of-2 + RM as predictor – can they help predict DILI?  Minjun Chen
8:55  Predicting DILI – an Inside-the-box analysis  Tom Jones
9:10  General discussion of Issues  ALL PRESENT
9:40  coffee break
10:10  DILI-sym initiative  Paul Watkins
10:30  European Quantitative Toxicology (EQT) – liver, kidney, heart, GI tract  Jim Stevens
10:50  MIP-DILI (mechanism-based integrated prediction of DILI)  Chris Goldring
11:10  Drug-induced liver injury leading to acute liver failure 2017  Will Lee
11:30  General discussion of Issues  ALL PRESENT
12:00  lunch break

1:00 SESSION IV  Consortia for Best Practices to Reduce DILI
Moderators: Paul Watkins and Gyongyi Szabo

1:00  The IQ DILI Initiative  Arie Regev
1:20  The IQ DILI working group on post-marketing risk assessment  Frank Czerwiec
1:40  SAFE-T Consortium  Gerd Kullak-Ublick
2:00  LiverTox update and prospects  Jay Hoofnagle
2:20  Expert judgment for causality assessment  Skip Hayashi
2:40  Is there a general mechanism for DILI? Do we need to know it?  Neil Kaplowitz
2:55  General Discussion of Issues  ALL PRESENT
3:25  refreshment break
3:40  Chinese DILIN experience  Yimin Mao
4:00  Who speaks for the prescribing physicians?  John Senior
4:20  General Discussion of Issues  ALL PRESENT
5:00  Adjourn

Note: Titles may be subject to changes between now and the time of the meeting.

Registration for the June 2017 Conference
Contact: Critical Path Institute, Tuscon AZ: 520-647-8376
Register Now: http://www.cvent.com/d/qvghcw/4W
Registration: $700 pharmaceutical industry employees; $350 academic and regulatory participants
Website: https://c-path.org/category/events

Please make lodging reservations on your own at The College Park Marriott Hotel and Conference Center, for those attending the DILI Conference. 301-985-7000 or www.marriott.com

Book your group rate for FDA Hepatotoxicity Meeting

{Copies of slides shown and transcripts of speakers’ comments and discussions will be posted four weeks after the conference at: www.aasld.org → Events and Professional Development, Drug-Induced Liver Injury Conferences. Previous conference agendas, slides, and comments may be seen at the same site.}