7th DIA Cardiac Safety Workshop in Japan

Leading into a New Era of Cardiovascular Safety Assessment

October 25-26, 2018
Nihonbashi Life Science HUB | Tokyo
DIAglobal.org/CSJP2018

OVERVIEW

There are ongoing discussions surrounding cardiovascular (CV) safety assessments of drugs in development. Although the implementation of the ICH E14/S7B guidelines is considered a success, proarrhythmia risk assessment continues to be one of the most important and challenging issues in drug development. The proarrhythmia risk assessment regulatory paradigm entered a new era in 2015 with the release of the ICH-E14 Q&A R3 document, which allows the use of Concentration Response Modeling of QTc data in lieu of the E14 'by-time point' analysis as the primary basis for regulatory decisions. This revision effectively allows pharmaceutical sponsors to use routine early phase (SAD/MAD) studies, with intensive PK and QT data collection, to meet current regulatory requirements instead of the E14 mandated Thorough QT/QTc study.

Concomitantly, development of new non-clinical CV risk assessment strategies, such as the use of induced pluripotent stem cells (iPS) derived cardiomyocyte and *in silico* cardiac models have been making advances both in Japan and abroad.

In addition to the well documented proarrhythmia risk, other CV risks including those associated with drug-induced changes in blood pressure, cardiac function and cardiomyocyte (structure), have been recognized as important issues requiring attention and appropriate assessment during drug development.

Furthermore, the increasing importance of the emerging field of cardio-oncology, reflects the success of new cancer therapies in improving life expectancy of cancer patients on one hand, and the recognized CV risks of innovative anticancer drugs including molecular targeted therapies on the other hand. A wide range of cardiotoxicities associated with existing and new anticancer therapies were reported, including cardiomyocyte injury and heart failure, vascular injury and hypertension or thrombosis, accelerated coronary artery disease and proarrhythmia, amongst others.

In this workshop, we will invite clinical, industry and regulatory experts to discuss a range of hot topics, including: Non-clinical proarrhythmia risk assessment using iPS derived cardiomyocyte and *in silico* models such as CiPA, JiCSA and iSMART; Clinical proarrhythmia risk assessment models and the implementation of QTc Concentration Response Modeling in Japan and new ECG biomarkers; A research update and future directions for the assessment of cardiac contractile function; A cardio-oncology session including mechanism of drug-induced cardiotoxicity, and strategies for early detection and assessment of cardiotoxicity.

The 7th Cardiac Safety Workshop in Japan will provide a unique opportunity to learn of and discuss the current state and future directions of CV risk assessments and how to prepare for a new regulatory paradigm of cardiovascular safety assessments. We look forward to welcoming you to the workshop.

WHO SHOULD ATTEND

The program will benefit those with the following interests:

- Drug development and clinical research managers and associates
- Pharmaceutical physicians and medical directors
- Safety pharmacology and non-clinical scientists
- Drug safety and drug surveillance personnel
- Clinical pharmacology scientists
- Pharmacovigilance managers
- Regulatory affairs managers
- Biostatisticians
- Data managers
- IT/technology managers
- Outsourcing and marketing managers
- Decision makers in drug safety, including toxicology, pharmacology and compliance

Endorsement by The Japanese Society of oxicology, Japanese Society of Medical Oncology

Tabletop Exhibit Opportunities Available

For more information, contact DIA Japan
Tel: +81.3.6214.0574 | Fax: +81.3.3278.1313
Email: Japan@DIAglobal.org

Simultaneous Translation Available

PROGRAM CHAIR

Kaori Shinagawa, MD, PhD
Pharmaceuticals and Medical Devices Agency (PMDA)

PROGRAM VICE CHAIR

Katsuyoshi Chiba, PhD
Daiichi Sankyo Co., Ltd.

PROGRAM COMMITTEE

Naoki Furuyama, DVM, PhD
Takeda Pharmaceutical Company Limited

Yasunari Kanda, PhD
National Institute of Health Sciences

Yuji Kumagai, MD, PhD
Kitasato University Hospital

Boaz Mendzelevski, MD
Cardiac Safety Consultants Ltd.

Atsushi Sugiyama, MD, PhD
Toho University Faculty of Medicine

Kyosuke Takeshita, MD, PhD, FAHA
Saitama Medical Center, Saitama Medical Universityl

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Drug Information Association
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9:30-10:00 REGISTRATION

10:00-10:10 WELCOME AND OPENING REMARKS

Akio Uemura, PhD
Senior Vice President & Managing Director, DIA Japan

Kaori Shinagawa, MD, PhD
Senior Scientist for Clinical Medicine, Office of New Drug II, Pharmaceuticals and Medical Devices Agency (PMDA)

10:10-12:10 SESSION 1 (PART 1)

Clinical Proarrhythmic Risk Assessment

SESSION CO-CHAIRS

Boaz Mendzelevski, MD
Cardiac Safety Consultants Ltd.

Kaori Shinagawa, MD, PhD
Senior Scientist for Clinical Medicine, Office of New Drug II, Pharmaceuticals and Medical Devices Agency (PMDA)

Regulatory Perspective for Clinical Proarrhythmic Risk Assessment
Kaori Shinagawa, MD, PhD
Senior Scientist for Clinical Medicine, Office of New Drug II, Pharmaceuticals and Medical Devices Agency (PMDA)

Differentiating Drug-Induced ion Channel Effects on the ECG: Potential Role of the ECG under CiPA
(Presentation via Internet)
Jose Vicente, PhD
Staff Fellow, Division of Cardiovascular and Renal Products, Office of Drug Evaluation I, Office of New Drugs, Center for Drug Evaluation and Research, U.S. Food and Drug Administration (FDA)

Regulatory Perspective for CR Modeling in Early Phase Studies and Other Biomarkers for Clinical Proarrhythmic Risk Assessment
Krishna Prasad, DrMed, MD, MRCP, FRCP
Group Manager (CardioVasc, Oncology, and Antiinfective Product Teams), Medicines and Healthcare products Regulatory Agency (MHRA)

Experience from QT Assessment Using Concentration-QTc Modeling of Early Phase Studies
Börje C. Darpö, MD, PhD
Chief Scientific Officer, Cardiac Safety, ERT

Effects of Moxifloxacin on the Proarrhythmic Surrogate Markers in Healthy Subjects: Exposure-Response Modeling using ECG Data of Thorough QT/QTc Study
Atsushi Sugiyama, MD, PhD
Professor and Chairman, Department of Pharmacology, School of Medicine, Toho University Faculty of Medicine

Experience with CR Modelling across Different Types of Early Phase Clinical Trials
Jörg Täubel, MD, FFPM
Chief Executive Officer, Richmond Pharmacology Ltd.

12:10-13:30 LUNCH

13:30-14:00 SESSION 1 (PART 2)

Clinical Proarrhythmic Risk Assessment

SESSION CO-CHAIRS

Boaz Mendzelevski, MD
Cardiac Safety Consultants Ltd.

Kaori Shinagawa, MD, PhD
Senior Scientist for Clinical Medicine, Office of New Drug II, Pharmaceuticals and Medical Devices Agency (PMDA)

Panel Discussion
PANELIST
All speakers in Session 1 except Dr. Jose Vicente

14:00-16:00 SESSION 2

Non Clinical Proarrhythmic Risk Assessment

SESSION CO-CHAIRS

Katsuyoshi Chiba, PhD
Senior Director and Head, Group III, Medicinal Safety Research Laboratories, Research Function, R&D Division, Daiichi Sankyo Co., Ltd.

Yasunari Kanda, PhD
Head of Division of Pharmacology, National Institute of Health Sciences

Keynote Lecture:
Prediction and Quantification of Torsadogenic Potential Using Classical and New Assay Models
Atsushi Sugiyama, MD, PhD
Professor and Chairman, Department of Pharmacology, School of Medicine, Toho University Faculty of Medicine

CiPA: Validation Efforts and Update
Gary Gintant, MA, PhD
Research Fellow, AbbVie Inc.

JiCSA Update: Proarrhythmia Risk Assessment Using Human iPS Cell-derived Cardiomyocytes
Yasunari Kanda, PhD
Head of Division of Pharmacology, National Institute of Health Sciences

iSmart (investigation of in silico / in vitro model for Arrhythmogenic Risk Prediction) Update
Keiichi Asakura, PhD
Senior Scientist, Pharmacokinetics and Safety Assessment Department, Nippon Shinyaku Co., Ltd.

Panel Discussion
PANELIST
All speakers in Session 2

16:00-16:30 COFFEE BREAK

16:30-17:45 SESSION 3

Abstract Session 1

SESSION CO-CHAIRS

Naoki Furuyama, DVM, PhD
Takeda Pharmaceutical Company Limited

Yuji Kumagai, MD, PhD
Director of Clinical Trial Center, Kitasato University Hospital

Can We Rely on Automated ECG Machine Measurements for Clinical Trial Decisions?
Robert Kleiman, DrMed
Chief Medical Officer and Vice President, Global Cardiology, ERT

Heart Rate Correction When the Drug Affects Heart Rate
Georg Ferber
Statistical Consultant, Statistik Georg Ferber GmbH

Intensive QT Investigation as Standard Practice in Early Clinical Programs in Lieu of Thorough QT Study
Sanae Yasuda, PhD
Senior Director, Clinical Pharmacology, Medicine Development Center, Eisai Co., Ltd.

Evaluation of a Proposed Novel Biomarker, the JTpeak Interval, for Evaluation of Proarrhythmic Liability
Börje C. Darpö, MD, PhD
Chief Scientific Officer, Cardiac Safety, ERT

Influence of Food on QT, J-Tpeak and Tpeak - Tend Intervals
Jörg Täubel, MD, FFPM
Chief Executive Officer, Richmond Pharmacology Ltd.

17:45-19:30 NETWORKING RECEPTION

9:00-9:30 REGISTRATION

9:30-10:30 SESSION 4

Cardiovascular Safety in Oncology Drug Development: Mechanisms of Cardiotoxicity

SESSION CO-CHAIRS

Katsuyoshi Chiba, PhD
Senior Director and Head, Group III, Medicinal Safety Research Laboratories, Research Function, R&D Division, Daiichi Sankyo Co., Ltd.

Atsushi Sugiyama, MD, PhD
Professor and Chairman, Department of Pharmacology, School of Medicine, Toho University Faculty of Medicine

Drug-Induced Cardiac Toxicity: Translating Non-Clinical Observations into Early Clinical Investigation
Atsuhiko T. Naito, MD, PhD
Associate Professor, School of Medicine, Toho University Faculty of Medicine

Development and Standardization of in vitro Contractility Method Using Human iPS Cell-Derived Cardiomyocytes
Yasunari Kanda, PhD
Head of Division of Pharmacology, National Institute of Health Sciences

Molecular Pathways and Pathophysiology of TKI Induced Cardiotoxicity
Junichi Ishida
The University of Tokyo Hospital

10:30-10:45 COFFEE BREAK

10:45-12:15 SESSION 5

Strategies for Early Detection of Cardiotoxicity

SESSION CO-CHAIRS

Atsushi Sugiyama, MD, PhD
Professor and Chairman, Department of Pharmacology, School of Medicine, Toho University Faculty of Medicine

Kyosuke Takeshita, MD, PhD, FAHA
Department of Clinical Laboratory Medicine, Saitama Medical Center, Saitama Medical University

Integrated Approach to Early Detection of Drug-Induced Cardiotoxicity
Hiroshi Akazawa, MD, PhD
Lecturer, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo

Imaging Biomarkers for Early Detection of Drug-Induced Cardiotoxicity
Kyosuke Takeshita, MD, PhD, FAHA
Department of Clinical Laboratory Medicine, Saitama Medical Center, Saitama Medical University

Preclinical Human Contractility Safety Testing
Najah Abi Gerges, PhD
Vice President, Research & Development, AnaBios Corporation

Panel Discussion

PANELIST
All speakers in Session 4 and 5

12:15-13:30 LUNCH

13:30-15:10 SESSION 6 (PART 1)

Strategies to Assess, Prevent and Mitigate Oncology Drugs Cardiotoxicity

SESSION CO-CHAIRS

Yuji Kumagai, MD, PhD
Director of Clinical Trial Center, Kitasato University Hospital

Boaz Mendzelevski, MD
Cardiac Safety Consultants Ltd.

Cardiovascular Safety Assessments of Oncology Drugs in Clinical Development
Boaz Mendzelevski, MD
Cardiac Safety Consultants Ltd.

Important Adverse Effects of Molecular-Targeting Drugs in Aspects of Cardio-Oncology
Manabu Minami, MD, PhD
Institute for Advancement of Clinical and Translational Science (iACT), Kyoto University Hospital

TKI Induced Cardiotoxicity and Drug-Induced Thrombosis
Wataru Shioyama, MD, PhD
Deputy Manager, Department of Cardiovascular Medicine, Onco-Cardiology Unit, Osaka International Cancer Institute

Oncology Drug-Induced Cardiotoxicity: Strategies to Assess, Prevent and Mitigate Cardiotoxicity Pre- and Post-Approval
Krishna Prasad, DrMed, MD, MRCP, FRCP
Group Manager (CardioVasc, Oncology, and Antiinfective Product Teams), Medicines and Healthcare products Regulatory Agency (MHRA)

Cardio-Oncology from the Regulator's Perspective
Hitoshi Kanno, MD, PhD
Reviewer, Office of New Drug V, Pharmaceuticals and Medical Devices Agency (PMDA)

15:10-15:40 COFFEE BREAK

15:40-16:10 SESSION 6 (PART 2)

Strategies to Assess, Prevent and Mitigate Cardiotoxicity

Panel Discussion

PANELIST
All speakers in Session 6

16:10-16:40 SESSION 7

Abstract Session 2

SESSION CO-CHAIRS

Yasunari Kanda, PhD
Head of Division of Pharmacology, National Institute of Health Sciences

Kaori Shinagawa, MD, PhD
Senior Scientist for Clinical Medicine, Office of New Drug II, Pharmaceuticals and Medical Devices Agency (PMDA)

A Case of Spontaneous Smoking Echo in a Patient with Bladder and Pancreatic Cancer - Detection of Prothrombotic Status with Echocardiography
Takako Morooka
Department of Medical Technique, Nagoya University Hospital

Blood Pressure Monitoring in Clinical Trials - from Efficacy to Safety Endpoints - Design and Technology Considerations
Jeff Heilbraun, MS
VP Strategic Development, Bioclinica

16:40-17:00 CLOSING REMARKS

Katsuyoshi Chiba, PhD
Senior Director and Head, Group III, Medicinal Safety Research Laboratories, Research Function, R&D Division, Daiichi Sankyo Co., Ltd.

Private Social Function Policy

DIA does not allow hospitality functions to be held during any DIA meeting sessions, scheduled exhibit hours, or social events. Therefore, the hours noted below are the only hours that are acceptable for hospitality functions.

Wednesday, October 24	All times are acceptable
Thursday, October 25	Before 8:00 and after 21:00
Friday, October 26	Before 8:00 and after 19:00

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NON-MEMBER	**Industry**	❑ **¥88,020**
	Government, Non Profit	❑ **¥45,900**
	Academia, Medicals	❑ **¥39,960**
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CANCELLATION POLICY: On or before October 18, 2018

Administrative fee that will be withheld from refund amount:
Member or Nonmember = ¥20,000
Government/Academia/Nonprofit (Member or Nonmember) = ¥10,000

Cancellations must be in writing and be received by the cancellation date above. Registrants who do not cancel by that date and do not attend will be responsible for the full registration fee paid.

Registrants are responsible for cancelling their own hotel and airline reservations. You may transfer your registration to a colleague at any time but **membership is not transferable**. Please notify DIA of any such substitutions as soon as possible. Substitute registrants will be responsible for nonmember fee, if applicable.

DIA does NOT allow registrants to pass name badges to others. DIA may ask attendees to show identifications, if necessary.

DIA reserves the right to alter the venue, if necessary. If an event is cancelled, DIA is not responsible for any airfare, hotel or other costs incurred by registrants.

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Signature Date

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