1st Think Tank Meeting on Cardiac Safety 2014 in Kirishima <Kirishima Meeting>

-From Follower to Player Against Galapagosization-

Date : Jan 11 (Sat) – 12 (Sun), 2014

Venue: Kirishima Iwasaki Hotel

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THE ORGANIZER

- The Japanese Safety Pharmacology Society

IN ASSOCIATION

- The Japanese Society of Clinical Pharmacology and Therapeutics

UNDER THE AUSPICES

- Ministry of Health Labour and Welfare
- Pharmaceuticals and Medical Devices Agency
- National Institute of Biomedical Innovation
- The Japanese Society of Electrocardiology
- The Japanese Pharmacological Society
- The Japanese Society of Toxicology

PROGRAM COMMITTEE

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OVERVIEW

At a FDA/CSRC/HESI-sponsored Think Tank Meeting held at FDA Headquarters on July 23rd, 2013, one of FDA speakers suggested new cardiac safety paradigm to propose “Abandon ICH E14 by July 2015” and “Revise ICH S7B by July 2016”. The current paradigm based on S7B and E14 has largely eliminated new drugs with torsadogenic potential entering the market. Since the current paradigm cannot necessarily provide precise information enough to predict proarrhythmic effects of new compounds, pharmaceutical company may have inappropriately discontinued the development of efficacious drugs solely due to their QT–interval prolonging property. Proposed new cardiac safety paradigm involves the Comprehensive *In Vitro* Proarrhythmia Assay (multiple ionic current measurement, *in silico* proarrhythmia prediction model, and usage of human ventricular myocytes) and careful Phase 1 ECG assessment.

Unfortunately, the Japanese regulatory, industry and academia were not directly represented in this discussion. There is a clear risk that Japan will again remain behind in this important debate on the new cardiac safety paradigm. To take the initiative and grow beyond Galapagosization, what goals should we set and how can we achieve them? We have to discuss and develop a strategy. It is critically important in the process to share information on our priorities and be conscious of the same problem in common to develop and propose revised/new ICH Guidelines based on the strategy.

iPS cell related technologies have been originated from Japan. Using iPS-cell derived cardiomyocytes, it may be possible to evaluate not only modulatory effects of a compound on ion channels but also its proarrhythmic potential, especially torsadogenic risk in a quantitative manner. We have to work in research and development in this important area from a leading position to establish de facto standard which will be introduced in future ICH Guidelines.

The objectives of Kirishima Meeting are as follows

To provide an opportunity for the Japanese regulatory, industry and academia to discuss about the latest cardiac safety issues

To show Japan’s strategic direction on future technology development

To produce and distribute worldwide a consensus report “Kirishima Declaration”

DAY 1 Saturday, January 11, 2014

OPENING

■ **13:30 - 13:45 Welcome, Agenda Overview and Raising Issues**

Atsushi Sugiyama, MD, PhD

Department of Pharmacology, School of Medicine, Faculty of Medicine, Toho University

■ **13:45 - 14:00 The mission of Kirishima Meeting**

Yuko Sekino, PhD

Division of Pharmacology, Biological Safety Research Center, National Institute of Health Sciences

SYMPOSIUM Ⅰ

SESSION 1 (14:00 - 15:30)
Clinical Cardiac Safety Evaluation
- ICH E14 and Beyond -

Moderators

Maki Ito, RN, MD, PhD

Department of Emergency Disaster and Critical Care Medicine, Emergency and Critical Care Center, Hyogo College of Medicine

Kaori Shinagawa, MD, PhD

Pharmaceuticals and Medical Devices Agency

■ **14:00 - 14:15 The Thorough QT/QTc Studies - Current Status in Japan -**

Yuji Kumagai, MD, PhD

Clinical Trial Center, Kitasato University East Hospital

■ **14:15 - 14:30 The Current Trends and Issues on Integrated Cardiac Safety**

Hiroyuki Fukase, MD, PhD

CPC Clinical Trial Hospital, Medipolis Medical Research Institute

■ **14:30 - 15:00 The New Paradigm for Proarrhythmia Assessment Without the TQT Study**

Philip T. Sager, MD, FACC, FAHA

Chair, Scientific Oversight Committee, FDA-Sponsored Cardiac Safety Research Consortium, USA

■ **15:00 - 15:30 PANEL DISCUSSION**

All speakers from this session

■ **15:30 - 15:45 BREAK**

SESSION 2-1 (15:45 - 17:15)
Future Perspectives on ICH S7B
- Key Directions for the New Paradigm -

Moderators

Kohei Sawada, PhD

Global CV Assessment, Eisai Co., Ltd.

Junko Kurokawa, PhD

Department of Bio-Informational Pharmacology, Medical Research Institute,

Tokyo Medical and Dental University

■ **15:45 - 16:15 The Current Status of Non-clinical Cardiac Safety in Japan**
- Focusing on Non-clinical Proarrhythima Models -

Atsushi Sugiyama, MD, PhD

Department of Pharmacology, School of Medicine, Faculty of Medicine, Toho University

■ **16:15 - 16:35 Assessment of drug effects on multiple ionic currents *in vitro* & *in vivo***

Haruaki Nakaya, MD, PhD

Department of Pharmacology, Chiba University Graduate School of Medicine

■ **16:35 - 16:55 *In silico* Predictive Modeling in Cardiology**

Takashi Ashihara, MD, PhD

Department of Cardiovascular Medicine, Shiga University of Medical Science

■ **16:55 - 17:15 Regarding UT Heart Simulator**

Seiryo Sugiura, MD, PhD

Graduate School of Frontier Sciences, the University of Tokyo

■ **19:00 - 21:00 NETWORKING RECEPTION**

DAY 2 Sunday, January 12, 2014

SYMPOSIUM II

SESSION 2-2 (8:30 - 9:30)
Future Perspectives on ICH S7B
- Key Directions for the New Paradigm (iPS-cell Derived Cardiomyocytes for Cardiac Safety Pharmacology Studies) -

Moderators

Yuko Sekino, PhD

Division of Pharmacology, Biological Safety Research Center, National Institute of Health Sciences

Yasunari Kanda, PhD

Division of Pharmacology, Biological Safety Research Center, National Institute of Health Sciences

■ **8:30 - 8:50 New Approach with Human Induced Pluripotent Stem Cell Derived Cardiomyocytes**

Kohei Sawada, PhD

Global CV Assessment, Eisai Co., Ltd.

■ **8:50 - 9:10 Development of an *in vitro* Cardiac Safety Testing Using Human iPS Cell-derived Mature Cardiomyocytes**

Yasunari Kanda, PhD

Division of Pharmacology, Biological Safety Research Center, National Institute of Health Sciences

■ **9:10 - 9:30 Differentiation System of Cardiovascular Cells from iPS Cells**

Jun Yamashita, MD, PhD

Center for iPS Cell Research and Application, Kyoto University

■ **9:30 - 9:45 BREAK**

SESSION 3 (9:45 - 11:45)
Future Trends of Cardiac Safety Evaluations
- Focusing on ICH Guidelines -

Moderators

Atsushi Sugiyama, MD, PhD

Department of Pharmacology, School of Medicine, Faculty of Medicine, Toho University

Hiroyuki Fukase, MD, PhD

CPC Clinical Trial Hospital, Medipolis Medical Research Institute

■ **9:45 - 10:00 Future Perspectives on ICH E14 - No Longer Necessary? -**

Kaori Shinagawa, MD, PhD

Pharmaceuticals and Medical Devices Agency

■ **10:00 - 10:15 Future Perspectives on ICH S7B - *in vivo*, *in vitro* and *in silico* -**

Kentaro Ando, PhD

Department of Pharmacology, School of Medicine, Faculty of Medicine, Toho University

■ **10:15 - 10:30 Regulatory Science to Accelerate the Development of Innovative Medical Products**

Toshinari Mitsuoka

Department of Food Safety, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare

■ **10:30 - 10:45 Cardiovascular Safety Pharmacology Studies - Japan's Future Directions -**

Yuko Sekino, PhD

Division of Pharmacology, Biological Safety Research Center, National Institute of Health Sciences

■ **10:45 - 11:00 BREAK**

■ **11:00 - 12:00 Summary of Kirishima Meeting and the Next Step**

1) **Clinical Pharmacology Working Group**

Hiroyuki Fukase, MD, PhD

CPC Clinical Trial Hospital, Medipolis Medical Research Institute

2) **Computational (*in silico*) Safety Pharmacology Working Group**

Junko Kurokawa, PhD

Department of Bio-Informational Pharmacology, Medical Research Institute, Tokyo Medical and Dental University

3) **Stem Cell Safety Pharmacology Working Group**

Kohei Sawada, PhD

Global CV Assessment, Eisai Co., Ltd.

■ **12:00 - 13:00 LUNCH BREAK**

■ **13:00 - 13:30 Summary of Kirishima Meeting and the Next Step**

4) **Integrated Cardiac Safety Working Group**

Atsushi Sugiyama, MD, PhD

Department of Pharmacology, School of Medicine, Faculty of Medicine, Toho University

CLOSING

■ **13:30 - Closing Remarks**

Kaoru Sugi, MD, PhD

Division of Cardiovascular Medicine, Toho University Ohashi Medical Center