

Division of Clinical Pharmacology and Therapeutics

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General Summary

The Division of Clinical Pharmacology and Therapeutics was established in July 1995. The aim of the division is to investigate drug treatment, mainly in the area of internal medicine, whereas other departments of clinical pharmacology in Japan focus on registration trials, particularly phase I trials. Because a clinical laboratory where we had performed many human pharmacological studies became unavailable in 2003, we shifted our research from human studies to multicenter clinical trials and pharmacoepidemiological studies.

Research Activities

Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) have been widely used to treat hyperlipidemia. However, they also have adverse effects on muscle, the liver, kidneys, and other organs. To investigate the incidence of these adverse effects and anti-hyperlipidemic effects, we performed a study according to a case-cohort design in which detailed data were collected from all cases and from a subcohort representing 5% of all subjects. A full-scale study has been completed with a large sample size of 7,000 patients from 68 institutions. A paper describing this study has been published.

The above-mentioned statin study took a long time to complete. We organized a research group comprising academic and industrial organizations (Japanese Society for Pharmacoepidemiology, Japanese Society of Clinical Pharmacology and Therapeutics, Japan Association for Medical Informatics, Japan Society of Clinical Trials and Research, Federation of Pharmaceutical Manufacturer's Associations of Japan, Pharmaceutical Research and Manufacturers of America, and European Federation of Pharmaceutical Industries and Associations Japan) to make postmarketing studies more efficient by utilizing the Standardized Structured Medical-record Information eXchange (SS-MIX). The SS-MIX system was started in 2006 as a project supported by the Ministry of Health, Labour and Welfare for promoting the exchange of standardized medical information. The SS-MIX system will increase the efficiency of pharmacoepidemiological studies by identifying "new users" who started the drug after some period of nonuse. The "new user" design is often essential for unbiased results.

To raise the literacy of clinical trials among researchers we held "Clinical Trial Seminar" 4 times this year. The themes were as follows: Survival data analysis (April 2014), Conflict of interest in medical research (July 2014), How to prevent misconduct in clinical trials (August 2014), and Ethical guidelines for medical and health care research involving human subjects (January 2015).

An administrative office for registration trials was established in the hospital in February 1999, and the system for registration trials in the hospital has been reformed to meet the

demands of the new good clinical practice guidelines. Seven clinical research coordinators (CRCs) now facilitate clinical trials. The CRCs have started to help with both registration trials and investigator-initiated trials. The CRCs have been introduced into all registration trials since 2004; the quality and speed of these trials were much improved. As the introduction of CRCs into investigator-initiated trials increased, we invited CRCs from site management organizations to supplement CRCs involved in registration trials.

Publications

Ooba N¹, Sato T², Wakana A³, Orii T⁴, Kitamura M, Kokan A⁵, Kurata H, Shimodozono Y⁶, Matsui K⁷, Yoshida H, Yamaguchi T⁸, Kageyama S, Kubota K¹ (†*Grad Sch Med Univ Tokyo*, ²*Tokyo Univ Sci*, ³*MSD K.K.*, ⁴*NTT Med Ctr*, ⁵*Eli Lilly Jpn*, ⁶*Kagoshima Univ*, ⁷*Showa Univ*, ⁸*Tohoku Univ Grad Sch Med*). A prospective stratified case-cohort study on statins and multiple adverse events in Japan. *PLoS One*. 2014; **9**: e96919.

Kadokura T¹, Akiyama N¹, Kashiwagi A², Utsuno A¹, Kazuta K¹, Yoshida S¹, Nagase I, Smulders R³, Kageyama S (†*Astellas Pharma*

Inc., ²*Shiga Univ Med Sci*, ³*Astellas Pharma Global Dev Eur*). Pharmacokinetic and pharmacodynamic study of ipragliflozin in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled study. *Diabetes Res Clin Pract*. 2014; **106**: 50-6.

Reviews and Books

Kageyama S. Investigator-initiated clinical trials score and quality assurance (in Japanese). *Iyaku Janaru*. 2015; **51**: 51-5.