Clinical Research Support Center

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General Summary

The Clinical Research Support Center was founded in April 2014 to promote the proper conduct of clinical research. The center has the following functions: protocol planning, statistical analysis, monitoring, support for clinical research conduct, and education. We started consulting for clinical research in September 2014 and had 31 protocols of consultation from April 2015 through March 2016. Consultations were as follows: 15 protocols for protocol planning and statistics (objective of the research, study design, control arm, study participants and their recruitment method, randomization, primary endpoint and its rationale, procedure to avoid/reduce bias, data collection, stopping criteria, statistical analysis, analysis sets, and sample size calculations), 1 protocol for the application of intellectual property, 3 protocols for the response to reviewers after the submission of articles (including additional analyses), 2 protocols for development strategy, and 10 protocols for conducting statistical analysis. Consultations were requested by the Departments of Endoscopy, Anesthesiology, Neurosurgery, Orthopaedic Surgery, Radiology, Psychiatry, Dentistry, Pediatrics, Forensic Medicine, Otorhinolaryngology, Surgery (Division of Digestive Surgery), and Internal Medicine (Divisions of Diabetes, Metabolism and Endocrinology; Clinical Oncology/Hematology; Gastroenterology and Hepatology; and Cardiology), the Laboratory Animal Facilities, and students of the nursing master's degree course.

In cooperation with the Division of Clinical Pharmacology and Therapeutics we held a "Clinical Trial Seminar" 4 times to improve literacy about clinical trials among researchers. The themes were "Superiority trial and non-inferiority trial" "Equivalence trial," "Evolution of IRB and clinical trials," and "Clinical trial insurance for compensation to research subjects to meet the demand of Ethical guidelines for medical and healthcare research involving human subjects." We also held a "Biostatistics Seminar for Tomorrow" consisting of 2 basic courses and 2 advanced courses to promote appropriate trial designs and the application of biostatistical methods.

Ethical guidelines for medical and health research involving human subjects have been implemented since April 2015. In these guidelines the principal investigator is obliged to perform monitoring if interventional studies are invasive. To meet this demand we prepared standard operating procedures for monitoring. The monitoring is performed by clinical research coordinators themselves or by supported investigators.

We introduced a clinical research liaison system to facilitate clinical research. We requested departments conducting many clinical trials to assign liaison physicians. Liaison physicians are invited to participate with priority in the "Biostatistics Seminar for Tomorrow" and are expected to act as liaisons between the department to which they belong and the Clinical Research Support Center.

Research Activities

Statistical methods of analyzing competing risks data

In the analysis of survival data, an individual is subjected to an event due to only 1 of several distinct types of causes, and the occurrence of 1 type omits other types of causes, such as death due to stroke and death due to myocardial infarction. These event types are given the statistical term "competing risks." When the primary endpoint is the mean change/percent change of a variable, such as HbA1c or blood pressure, from the baseline to the planned end of the study and is repeatedly measured, a typical problem is missing data. Nowadays, intensive discussions are done about the problem of missing data, and an Addendum to the Statistical Principles for Clinical Trials of the International Conference on Harmonization has been started by its expert working group. We consider applying a method of analyzing data on competing risks in such a situation. We define an event of improvement on the measurement objectively and treat missing as a competing risk. We explored design in superiority trials and explored statistical methods in noninferiority trials.

To evaluate within patient consistency between measures, for example, pain intensities of patients are repeatedly measured with a visual analogue scale and an objective measuring device (Pain Vision, Nipro Co., Osaka) in clinical research, intraindividual coefficient of variations are compared between measures. The correlated samples and different interindividual variations due to different scales of the measures should be taken into account in statistical analysis. In such a situation, a statistical approach to compare the intraindividual coefficient of variations was proposed with the adjustment of covariates.

Publications

Kawamori R (Juntendo Univ Grad Sch Med), Kaku K(Kawasaki Med Sch), Hanafusa T (Osaka Med Coll), Ioriya K (Sumitomo Dainippon Pharma Co., Ltd.), Kageyama S, Hotta N (Chubu-Rosai Hosp). Clinical study of repaglinide efficacy and safety in type 2 diabetes mellitus patients with blood glucose levels inadequately controlled by sitagliptin. *J Diabetes Investig.* 2016; **7:** 253-9.

Kiyomi F[1], Nishikawa M, Yoshida Y[1], Noda K[1] ([1]Fukuoka Univ). Comparison of intra-individual coefficients of variation on the paired sampling data when inter-individual variations are different between measures. *BMC Resh Notes.* 2016; **9:** 115.