Developing an interactive mail registration and randomization system for clinical trials

Kanae Takahashi, Keiichi Yamamoto, Akiko Kada, Kunihiro Nishimura, Keiko Ohta, Yoshihiro Miyamoto, Hatsue Ishibashi-Ueda, Shigeki Kuwata, Haruko Yamamoto

Randomization is an essential requirement in confirmatory and comparative clinical trials. However, current computerized registration and randomization systems are expensive because specific case registration and randomization programs are required for each trial. We developed an interactive mail registration and randomization system only describing trial-specific information in an EXCEL® sheet, which can be adapted to various clinical trials. We believe our system will facilitate the execution of multi-center investigator-initiated clinical trials with limited budgets.

I. BACKGROUND

When executing clinical trials, it is necessary to make properties equal among the treatment groups to maintain comparability at the beginning of the study. The method for this purpose is randomization, which is an essential requirement in confirmatory and comparative clinical trials [1]. Various information technologies are currently used to improve the efficiency of clinical trials, and computerized registration and randomization systems are already in use in various clinical trials. Two conventional methods currently in use are the interactive web registry system (IWRS), which uses WEB data entry, and the interactive voice registry system (IVRS), which uses voice response. These methods have the advantage of enabling automatic registration for 24 hours, but are generally expensive, due to the need to customize registration and randomization computer programs for each trial. Moreover, they are often cost-prohibitive for smaller scale investigator-initiated research with limited budgets [2]. In addition, while clinical trials are governed by international standards, registration forms and eligibility criteria for case registration have not yet been completely standardized [2]. In order to minimize costs and improve the efficiency of clinical trials, a registration system is required that does not need to be customized to a specific trial and that enables automatic registration and randomization. The purpose of this study was to demonstrate an interactive mail registration and randomization system and to discuss its feasibility for use in clinical trials.

II. METHODS

We developed an interactive mail registration and randomization system. In this system, the minimization method is used to execute randomization [1], and randomized logics are developed using SAS®. In this system, trial specific-information (e.g., trial name, random seed, allocation probability, upper limitation of imbalance in the number of patients between groups, number of inclusion criteria, number of exclusion criteria, number of identification variable, prognostic factor, levels within a factor, weight of each factor, and treatment arms) are described in an EXCEL® sheet. These parameters are imported automatically by the system and are used for allocation. The system automatically generates CSV files from electronic case registration forms submitted by investigators by e-mail in PDF or EXCEL® formats. These data are imported to SAS®, and registration is achieved automatically using the following procedure: (1) it is checked if the case is already registered; (2) the case is checked against the eligibility criteria; (3) a subject number is allocated; and (4) randomization is executed. The results of the registration and randomization processes are output in PDF format and sent to the investigator by e-mail automatically.

III. RESULTS AND DISCUSSION

We conducted tests based on the predefined criteria. In addition, we carried out 100 simulated randomizations in hypothetical trials. No unexpected problems were encountered, including the validity of the randomization. This system is adaptable to various clinical trials, including multi-center trials, by describing trial specific information in an EXCEL® spreadsheet. By reducing the cost of registration and randomization of future clinical trials, our system will facilitate the execution of multi-center investigator-initiated clinical trials with limited budgets.

REFERENCES
