瀬戸内国際臨床試験／臨床薬理阿蘇九重
合同カンファレンス　論説

臨床試験におけるアダプティブデザイン*1

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Adaptive designs in clinical trials: An overview

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Abstract

Adaptive designs started from an introduction of group sequential designs. They allow some modifications in the trial design as well as stopping the trial early. It is based on the Bayesian perspective. It may be useful in many aspects but the study integrity and validity can be easily violated. Therefore, statistical and operational bias should be evaluated in advance and minimized as much as possible. Planning a possible amendment at interim occasions should be pre-specified in the protocol. The article overviews some merits and deficiencies related to the adaptive designs. It illustrates many examples of the adaptation in the allocation ratios, eligibility criteria, and study hypotheses. It also addresses a regulatory perspective by exhibiting the U.S. Food and Drug Administration guidance issued in 2010. Adaptation under the blinded review is well understood generally. Yet, if the adaptation is based on the interim analysis in an un-blinded condition, it is not well understood except the safety concern. Simulation studies are ongoing in the un-blinded cases to evaluate systematic and chance errors from statistical viewpoints. Finally, it illustrates two real examples of the adaptation in clinical trials.

Key words
clinical trial design, bias, statistics, guidance

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