Comments on Adaptive Design

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Experience in the PMDA

- There are more than 30* cases with adaptive design in clinical trial consultation meetings in the PMDA
  - Sample size re-estimation
  - Combination of learning and confirm phase
  - Adaptive dose-ranging
- The number of cases is increasing very gradually compared with a few years ago.
- Although oncology area is still the key area that adaptive design proposed, the number of cases in other areas is also increasing.

*Not including group sequential trials

Key questions

- Why we need the adaptive design in this situation?
  - Degree of lack of prior information
  - Balance of risk (error, bias) and benefit (efficiency?)
- Clinical trials with adaptive design in the clinical data package
- Possibility of introducing bias

Operational errors

- Several non-adaptive cases with operational errors
  - Program for randomization or statistical analysis
  - Information leakage to Inappropriate person
- Possibility of communication errors in the environment with role specialization
  - On the other hand, a degree of separation will be important in some situations, for example, situation with the person who should be independent of other persons involved

Guidance on DMC

- Japanese guidance document on Data Monitoring Committees (DMC) is now under consideration
  - Increasing cases with group sequential trials and large scale trials
  - Importance (necessity in some cases) of safety monitoring and careful implementation

Future tasks

- There seems to be the possible (suitable) situation for using adaptive design
- Appropriate use of adaptive design
  - Characteristics of the disease and drug
  - Sufficiency of prior information
  - Expected clinical data package
  - Information sharing and training