Bioequivalence Studies in Multiple Groups

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Outline

- BE Studies with Multiple Groups
- BE Assessment for Studies with Multiple Groups
- Treatment by Group Interaction
- Statistical Analysis Plan (SAP)
- Key Message

BE studies with Multiple Groups

- Multiple sources of groups (subgroups, cohorts)
- Recommend to minimize the group effect in PK BE studies

✓ Dose all groups at the same clinic
✓ Recruit subjects from the same enrollment pool
✓ Randomly assign subjects to group and treatment arm
✓ Follow the same protocol criteria and procedures
✓ Assign equal sample size to each group

BE Assessment for Studies with Multiple Groups

- BE - overall treatment effect in the whole study population
- BE assessment in the whole study population:

✓ Generally: w/o treatment by group interaction

✓ However, applicants may use other pre-specified models

✓ Complicated scenarios - discuss with the agency

Treatment by Group Interaction

- Assessment of interaction – important
  - especially when first four criteria not met
  - and PK BE is pivotal for drug approval

- If treatment-by-group interaction is significant

✓ Heterogeneity: carefully examined & interpreted with care

✓ If treatment effect varies greatly among the groups:
⟹ appropriate further explanation, analysis, interpretation

SAP

- Fully pre-specify statistical methods and models
- for primary BE analysis
- If treatment-by-group interaction applicable

- Model should reflect multigroup nature:
  e.g., period (group) in a crossover BE study

- Combine centers with very few subjects:

✓ Pre-specify combination rules

✓ Sensitivity analysis is recommended

Key Message

Pre-specify in detail in your Statistical Analysis Plan how to handle multiple groups