

PhRMA Adaptive Design Workshop

Session D: Dose Finding

Co-leaders

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Dose-finding session

Goal

- Discuss adaptive designs in dose-finding studies

Two causes of delayed approval or non-approval

- Poor dose selection in early phase studies
- Phase III designs do not utilize information from early phase studies

Objective of adaptation

Characterize of (safety and efficacy) dose-response functions

Facilitate dose selection

- Simulation study by PhRMA Adaptive Dose-Ranging Studies working group
- Conclusion: Dose selection is the more challenging task

Dose selection

Clinical trial sponsors are encouraged to include multiple doses from the therapeutic window in confirmatory studies

Build adaptive strategies aiming at defining a therapeutic window based on continuously accumulating efficacy and safety information

Therapeutic window

Based on utility function with efficacy and safety components

- Component weights are driven by clinical considerations

Profile of the utility function depends on the drug and disease

Role of safety assessment

- Choice of the dose depends heavily on evidence of toxicity in oncology studies
- May be difficult to perform in smaller early phase studies