

Introduction

Drug developers are under pressure to balance cost with agility and get promising therapies to patients sooner. Traditional clinical development programs follow a phased approach (phase I-IV) and generally require commitment of resources to trials for years. Adaptive trial design offers an alternative approach to design protocols with pre-planned adaptations that improve the chances of making the correct decision at the earliest possible timepoint in a clinical trial and increase drug development efficiency. This poster reviews commonly used adaptive trial designs. We will share a programmer’s experience using recent adaptive trials to highlight opportunities and lessons learned in the conduct of these trials (e.g. key stakeholders to consider when planning these trials, collaboration with vendors, documentation, dry runs, handoffs between blinded and unblinded teams, archiving data and communications etc.).

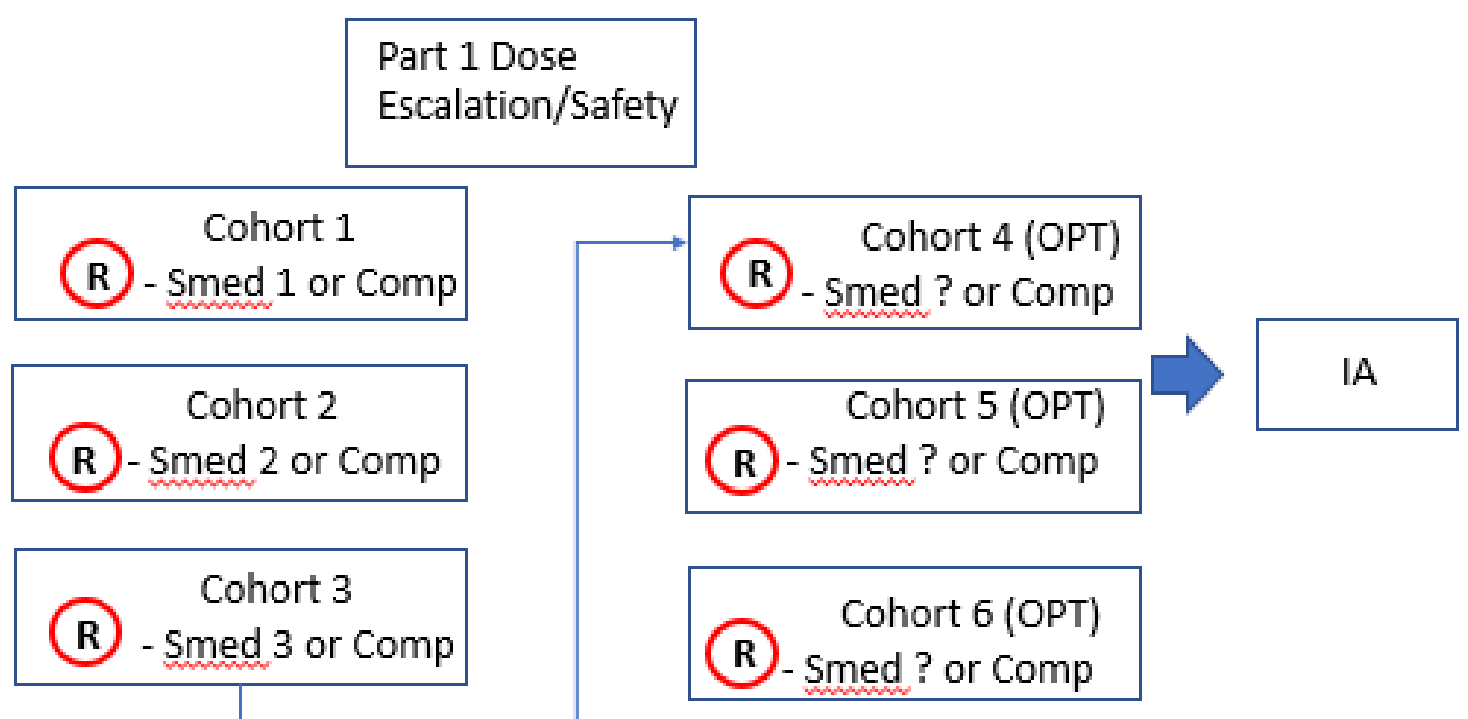
What is Adaptive Trial Design?

¹ “...An adaptive design is defined as a clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial.”

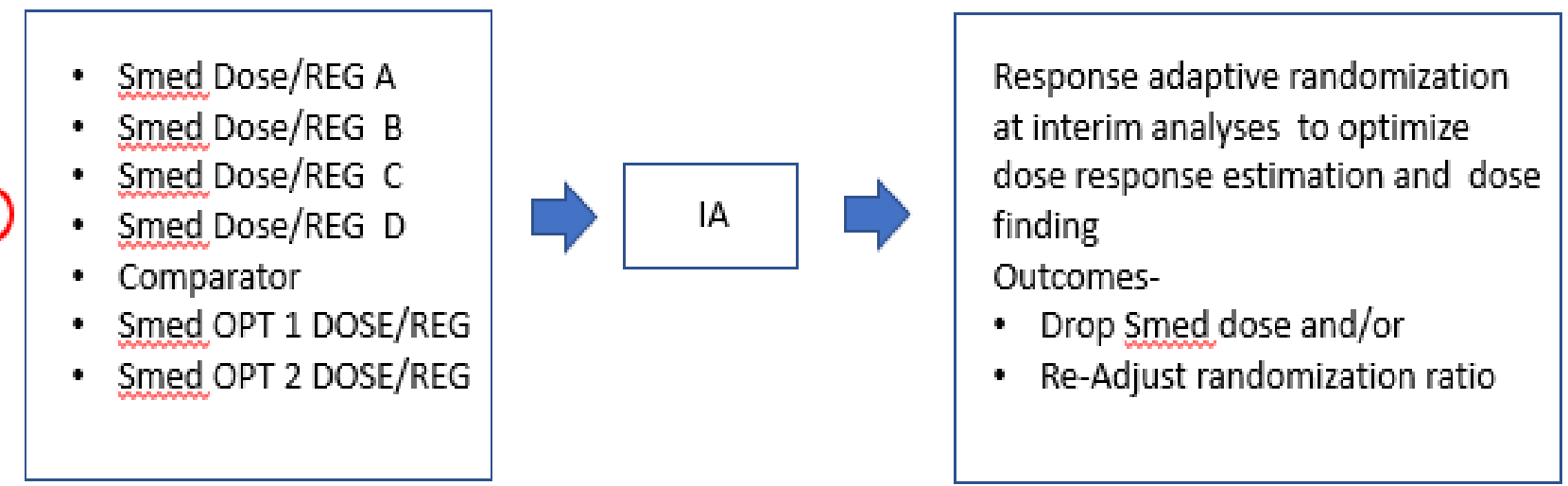
Advantages:

- Achieves statistical efficiency by detecting true treatment effect
- Potentially improves ethical conduct by stopping trial early for futility or superior efficacy
- Increases 'buy in' with stakeholders (sponsors, patients etc.)
- Offers generalizability and understanding of drug effects

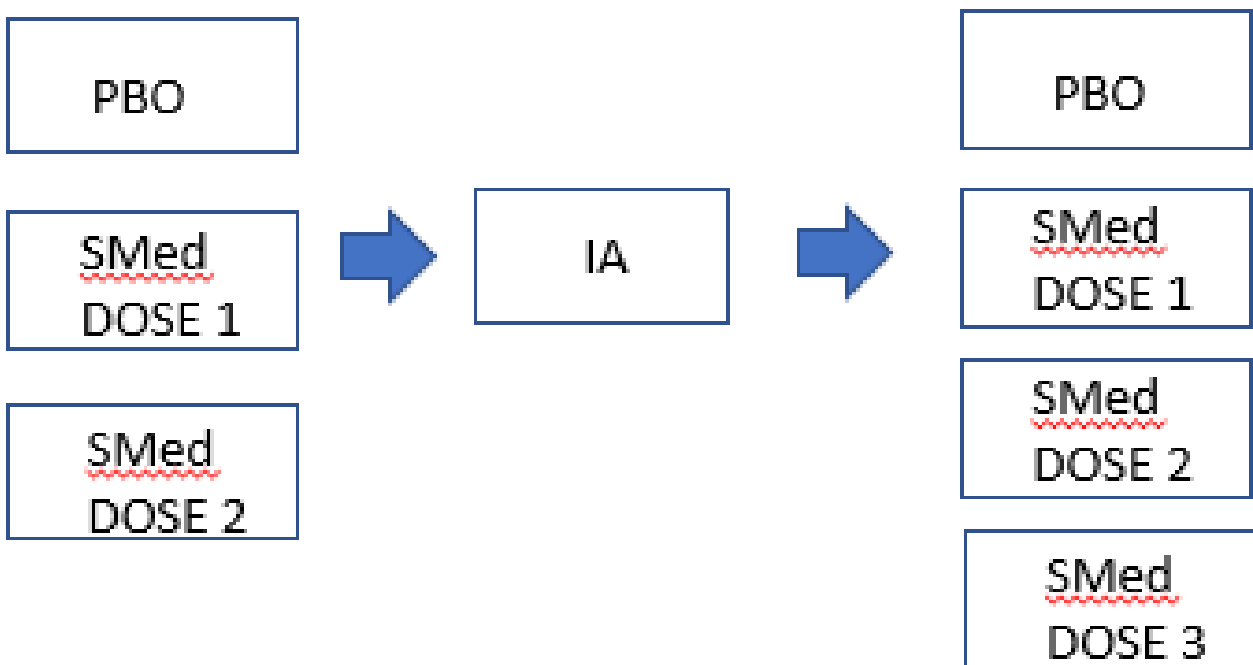
Part 1 Dose Escalation/Part 2 Dose Response



Response Adaptive Randomization



Addition of a Dose



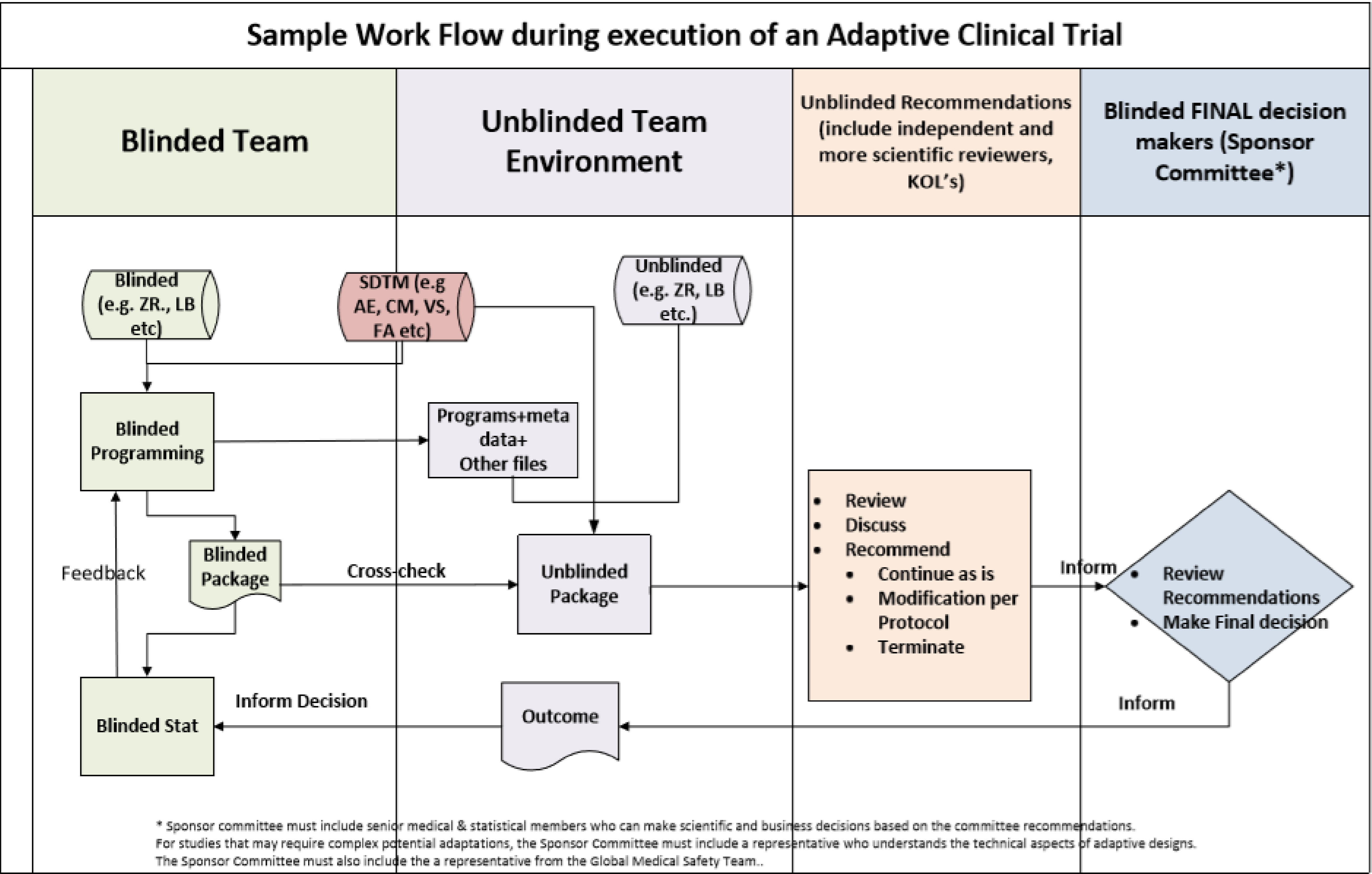
Ⓡ : Randomization; Smed: Study Medication; Comp: Comparator; IA: Interim Analysis; PBO: Placebo; REG: Regimen (e.g. QD, BID etc.); OPT: Optional

GEMS

- Use almost 'Real Time' data for reporting and decision making
- Collaboration between internal and external counterparts
- Clear documentation on process, sequestered environment access execution and archiving plan
- Outcomes help make informed Go/No Go decision for program to move forward
- Ability to leverage global team across time zones
- Planning (Set up early, conduct Dry Runs)

OPPORTUNITIES

- Detailed planning that is in compliance with company SOPs
- Stable and timely data format, structure and transfers
- Robust review and QC of deliverables by both blinded and unblinded teams
- Flexibility
 - To make and QC quick updates during production run
- Blinded team on standby for questions
- Extended team (IT, vendors, CROs) available for updated data or support



Conclusions

- Adaptive trial designs and complex innovative designs such as 'Basket/'platform' trials are increasingly being implemented to gain efficiencies and reduce costs by applying "kiss and kill" method
- Collaborations and flexibility within cross functional teams to think "out of the box," anticipate issues and find solutions are key to success of these trials
- Programmers and statisticians play a critical role in generating analyses that enable informed decision making

Reference

¹<https://www.fda.gov/media/78495/download>