CALYX™

CASE STUDY

Designing an Adaptable IRT System for Effective Platform Trials

SITUATION

PRINCIPLES OF A PLATFORM TRIAL

Clinical trial with a single master protocol to which multiple sub-protocols are associated over time.

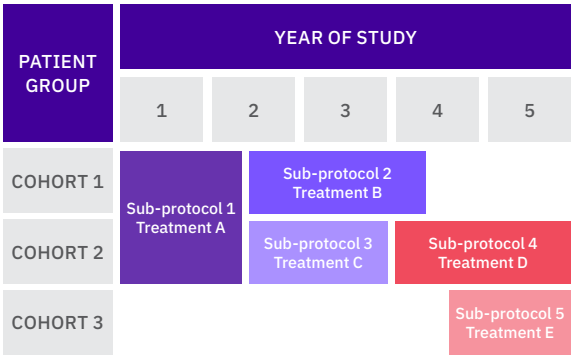
- Trial model allows new treatment development gained during the active running of the master protocol to be introduced and tested as a new sub-protocol, accelerating the development cycle.
- Each sub-protocol can define a new treatment, patient group, and visit schedule.
- An "open treatment" is an approved treatment at a particular site that has yet to meet its randomization target.
- For any new sub-protocol added, a multi-center trial could require regulatory approval on a site-by-site basis during the recruitment phase.
- Any given site may not have an approval for all sub-protocols at the same time. As such, patients can only be randomized between the treatments that their site has approval for, provided that the recruitment target has not been reached for these treatments.

CHALLENGE

MULTIPLE SUB-PROTOCOLS MAY BE ACTIVE AT ANY TIME

Adaptive nature to the randomization must be considered

- Not all sub-protocols are defined at the start of the study, or at the point when the IRT goes live (see Fig 1).
- IRT must have the flexibility to anticipate future sub-protocol treatments to be included, but also an efficient change management process for any unforeseen adaptation a future sub-protocol may require.



ACTION

HOW CAN IRT CONSULTING AND DESIGN SUPPORT PLATFORM TRIALS?

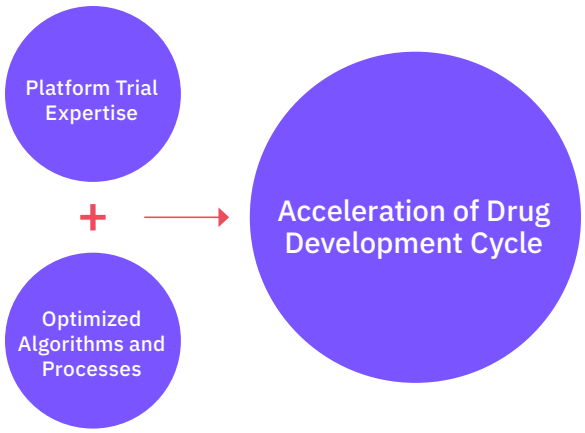
- Aim of randomization process is to make a random assignment among the open treatments.
- Complex capping of individual treatments/sub-protocols is paramount to control enrollment in each sub-protocol.
- Randomizing between the "open treatments" at sites requires accurate tracking of each site's sub-protocol approval status, otherwise there is a risk of protocol deviations.
- A well-designed randomization algorithm should allow "skipping" of closed treatment arm records, to ensure randomization among the open arms.
- Storing the available treatments during each randomization provides an audit trail that allows traceability and "reproducibility" of the process for regulatory or validation scrutiny at any point in the trial.

RESULT

KEY PRINCIPLES TO APPLY TO IRT IN SUPPORT OF PLATFORM TRIALS:

- Site approval menu for all available sub-protocols
- Capping automatically closing randomization into sub-protocols when target enrollment is reached
- Blocked randomization list including spare records/ placeholders for future sub-protocol release
- Ability to use probabilities within the randomization algorithm
- Use audit trail to record which treatment arms were open during each randomization and to show why block entries were skipped (closed treatment or one that was not open/approved yet)
- Randomization algorithm must ensure that skipping is not applied for a lack of medication[1]
- Efficient change management process for the unforeseen new requirements of a future sub-protocol

Calyx has the experience and ability to build effective IRT solutions for platform studies. Our processes and technology allow adaptability for requirements that are not planned up front.



Contact hello@calyx.ai to learn how Calyx's expertise in IRT can ensure your trials' success.

1. McEntegart D. Forced randomization when using interactive voice response systems. *Appl Clin Trials* 2003;12(10):50-58. http://www.clinphone.com/files/item91.aspx Accessed 28 Aug 2019.

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