Paper TA04

Are Platform Studies the Need of the Hour for Oncology Trials?

Vidya Muthukumar, IQVIA, Durham, NC 27503

ABSTRACT

In the fast-changing, cost-conscious clinical trials industry, platform trials are slowly becoming the need of the hour, especially for oncology studies. Sponsors are often looking to gain level-playing fields to maintain a cost equilibrium for clinical trials. Platform trials are set up to study diseases in specific therapeutic areas, rather than specific interventions. Trials can continue indefinitely, adding new arms to test new therapies, or discontinue existing ones as soon as it becomes clear the drug is ineffective or harmful, and substitute the control arm for a new standard-of-care. The randomization process can be amended so that new participants are more likely to receive a better performing therapy. The key features of platform trials are their scope and adaptability. They are designed to evaluate multiple therapies. Rather than test drugs one at a time, one could test them all at once; and get results quickly to make informed decisions.

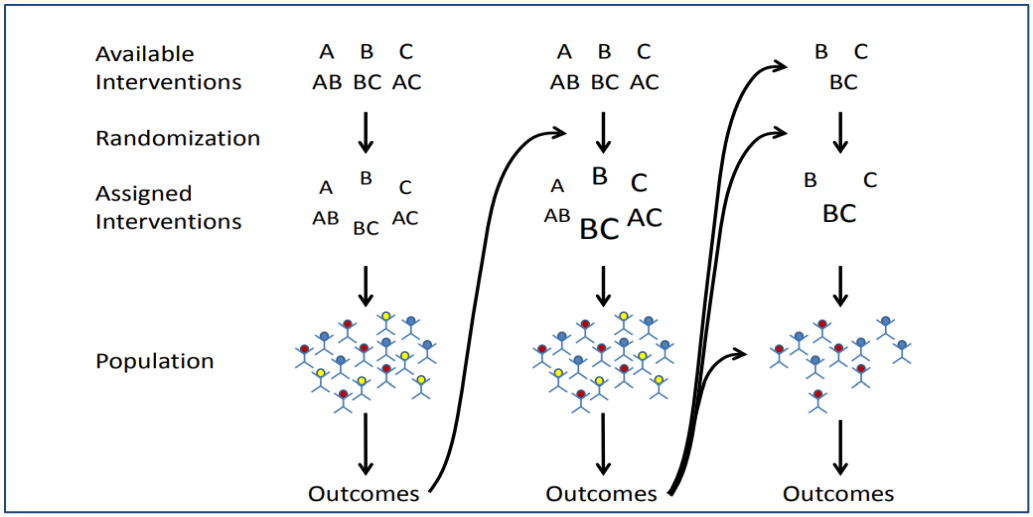
INTRODUCTION

A traditional clinical trial typically takes two years to design, create infrastructure, begin enrolling patients until final closeout. A platform trial, on the other hand, is built with a master protocol, to allow multiple therapies to be investigated in the single trial, being added continuously, all with shared infrastructure. A platform trial, also referred to as multi-arm multi-stage (MAMS), allows multiple arms to share a common control, share the common infrastructure of the trial, and it allows for better treatment of patients in the trial.

WHAT IS A PLATFORM TRIAL?

A platform trial is defined by the broad goal of finding the best treatment for a disease by simultaneously investigating multiple treatments, using specialized statistical tools for allocating patients and analyzing results. The focus is on the disease rather than any particular experimental therapy. A platform trial is often intended to continue beyond the evaluation of the initial treatments and to investigate treatment combinations, to quantify differences in treatment effects in subgroups, and to treat patients as effectively as possible within the trial.

During a platform trial, accumulating outcomes data can be used to adjust the randomization probabilities to preferentially assign better-performing treatment regimens to future patients. This approach, response-adaptive randomization, improves the outcomes of study participants treated within the trial, increases the available information on treatment effects and adverse effects for the most effective treatments, and shortens the evaluation time for the best therapies.



In the above example of an adaptive platform trial, three treatments (A, B, and C) and all combinations (AB, BC, and AC) were assessed in a population of patients that included three subtypes of the disease (“blue,” “red,” and “yellow”). When the study started, randomization was balanced between all possible treatments and all patient subtypes were treated similarly. After a period of time, it appeared that BC was having a greater effect than the other treatments and, to a lesser extent, so were B, C, and AC. Thus, subsequent randomization enriched the number of patients assigned to receive BC, shown by the bigger font, and B, C, and AC. After the trial continued further, analysis revealed that treatment A and its combinations were not effective in any subgroup and subgroup “yellow” was not effectively treated in any arm, so patients were no longer randomized to receive any combination including treatment A and the “yellow” subgroup was discontinued from further enrollment. At the end of the trial, not shown in the figure, the combination treatment BC could graduate from the trial based on evidence of benefit in the “blue” subtype of disease, to be recommended for clinical use, or for further evaluation in a separate phase III trial.

BENEFITS OF PLATFORM TRIALS FOR DATA MANAGEMENT

Platform trials are emerging as novel trial designs as a result of recent advances in precision medicine that have motivated novel trial designs, most notably the idea of master protocol (e.g., platform trial, basket trial, umbrella trial), for the evaluation of molecularly targeted cancer therapies. In early-phase cancer trial designs, for ex., focus is often on dose finding and treatment screening in the context of platform trials of molecularly targeted cancer therapies. Because most cancer trial designs have been developed for cytotoxic agents, these time-tested design principles hold relevance for targeted cancer therapies, and for this, a master protocol may serve as an efficient platform for safety and efficacy evaluations of novel targeted therapies. In that, data management that are well equipped to handle state-of-art simulation modeling techniques to identify dose-finding methods, futility screening, treatment selection, and early stopping rules, often help platform trials with outcomes decisions. Having flexible and adaptive trial designs in early phase oncology platform studies allows the review of emerging safety, PK, and PD data which can result in safer, more informed decision-making, lowering risks and improving overall subject safety effectively.

BENEFITS OF PLATFORM TRIALS FOR SPONSORS

To meet fit-for-purpose needs of early phase oncology studies, sponsors could benefit from considering three main criteria when deciding on collaborating on a master protocol for a platform trial:

1. Country/Site selection: Utilizing robust data for strategic planning of optimal country and sites is crucial. Early engagement can lead to a smart selection of sites that can help achieve first patient enrolled (FPI) as well as overall enrollment.
2. Start-up: Keeping the big picture in mind is important. Establishing FPI guidelines and consider conducting a site kick-off meeting to map out start-up plans. Effective communication with sites during start-up and employing technology to ease the burden of document review and delivery could be key deciding factors.
3. Data excellence and decision making: Implementing a well-defined cohort management plan with tech-enabled communication allows for transparency with sites. In addition, a proactive data cleaning strategy with clear expectations across the clinical, data management and site can help increase trial efficiency, speed and safety.

CONCLUSION

Platform trials can find beneficial treatments with fewer patients, fewer patient failures, less time, and with greater probability of success than a traditional two-arm strategy. In an era of sky rocketing costs for clinical trials, platform trials provide the innovation needed to efficiently evaluate modern treatments. Platform trials investigate the best treatment for a disease from a range of investigated options, rather than looking at an intervention to see whether it is better than a comparison – it is more “disease-focused" rather than "intervention-focused. Multiple stages of interim analysis allow the investigators to adjust the size of the sample, which means the trial may not run into a situation where it is suddenly discovered there was not enough enrollment to detect an unexpectedly small treatment effect.

For patients enrolled in a platform trial, the trial decreases the risk that they will be allocated to a control group (which is smaller) or to an ineffective treatment (which would be dropped from the study). This means that the benefits of participating are more equitably shared across the study population. It also means that - once you have finished studying an apparently ineffective treatment - you can keep using the already collected results and comparing them to new treatments in other arms added later, without having to expose another set of patients to the ineffective treatment.

REFERENCES AND PUBLICATIONS

https://classic.clinicaltrials.gov/ct2/results?cond=Oncology&term=platform+trials&cntry=&state=&city=&dist=
https://www.fda.gov/media/120721/download
https://www.fda.gov/about-fda/oncology-center-excellence/project-optimus
https://erj.ersjournals.com/content/50/4/1701655
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9756081/#tb0065
https://pubmed.ncbi.nlm.nih.gov/26908536/
https://pubmed.ncbi.nlm.nih.gov/34455953/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10260347/
https://pubmed.ncbi.nlm.nih.gov/34833129/
https://www.iqviabiotech.com/-/media/biotech/pdfs/library/white-papers/navigating-the-complex-oncology-landscape--iqvia-biotech-insight-brief.pdf?_=1705065636486
https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/global-oncology-trends-2023/iqvia-institute-global-oncology-trends-2023-forweb.pdf
https://www.nejm.org/doi/full/10.1056/NEJMoa1513749
https://www.frontiersin.org/articles/10.3389/fmed.2022.1037439/full
https://www.nature.com/articles/s44159-021-00012-0
https://www.nature.com/articles/s41591-022-01775-6
https://iris.who.int/bitstream/handle/10665/373129/9789240079670-eng.pdf?sequence=1

CONTACT INFORMATION

Author Name: Vidya Muthukumar
Company: IQVIA
Address: 2400 Ellis Rd Pod A, Level 4
Durham, NC 27503
Work Phone: +1-984-212-5831
Email: vidya.muthukumar@iqvia.com
Website: www.iqvia.com