PharmaVOICE

Drug Development Innovation: Increasing the Likelihood of Drug-to-Market Launch with Adaptive Trial Designs

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The current state of pharmaceutical drug development is not on a sustainable path forward. Many experts believe that the process is inefficient, lengthy and costly. The average time it takes to bring a drug to market has stagnated to nearly 12 years. The failure rate is high and often drugs fail in late stage which is costly in terms of time and resources. With mounting pressure on companies to bring affordable drugs to market, it has become imperative to confront these issues and implement innovations that could improve the process and bring about more promising results.

To address this issue, PAREXEL commissioned the Economist Intelligence Unit (EIU) to assess four clinical trial innovations, adaptive, patient-centric and precision medicine trials, and studies that use real-world data, to better understand how these innovations could improve the efficiency, productivity and sustainability of the drug development process and the likelihood of a successful drug launch. The key findings of this research and analysis were unveiled in a report: ***The Innovation Imperative: The Future of Drug Development,*** that revealed these innovations hold substantial promise in increased success rates of likelihood of drug-to-market launch and drug development sustainability.

Interestingly, innovations like adaptive trials aren't new; they have been around for decades. Yet despite their promise of decreasing patient recruitment time and increasing likelihood of drug to market launch, adaptive trials are used less than 1% in Phase II and Phase III trials.

Benefits of an adaptive trial design

Quite simply, adaptive clinical trials are studies that evaluate participant outcomes based on interim data and modify the parameters of the trial based on those observations. More specifically, adaptive trial designs incorporate pre-specified modifications into the protocol, allowing for changes to be made once the trial is in process based on interim data analysis, ultimately increasing the chances of the study succeeding. Researchers specify a set of criteria upfront that can be "adapted" as the trial progresses, depending on the results observed during an interim analysis. These protocol changes can include adjusting the sample size, drug dosage, patient population selection criteria and endpoint selection. This flexible approach is designed to reduce waste by allowing triallists to adapt the trial protocols based on emergent findings, where trials might otherwise be unsuccessful or terminated, and enables researchers to make informed decisions to redirect the study. A well designed and well-executed adaptive trial can maximize the information from the trial, improve efficiency, reduce overall development costs, and reduce the risk for participants and sponsors.

According to the EIU report, when adaptive trials are used specifically in oncology studies, drugs are more likely to be launched 81% of the time versus 68% of those developed without an adaptive design. Additionally, adaptive trials took 40% less time to recruit 100 patients (2.8 months versus the average 7 months to recruit 100 patients) and the study recruited 5% fewer patients (260) compared to non-innovative trials (271). Recruiting patients in less time enabled more time spent on the study itself.

Beyond adaptive trial designs as a proven innovation to benefit the drug development process are synthetic trials, otherwise known as external exploratory trials, which use external de-identified data for analyses that can establish early endpoints as predictors of long term clinical outcomes in early-stage trials to provide guidance on moving the trial forward, or not. While, synthetic trials differ from adaptive trials, synthetic trials *can* be adaptive. For example, if researchers conduct an interim analysis on study performance, they could potentially modify the design of the study by increasing the sample size, alter the dosage, etc. for the duration of the study if needed.

Barriers to adoption

Although adaptive trials have an overall positive impact on the drug development process, the industry faces several challenges that impede innovation adoption. The EIU report revealed that one of the biggest challenges is workforce readiness, where researchers lack the skills or expertise needed to design or analyze trial data. By providing the necessary training and tools to researchers, adoption of adaptive trial designs would be higher and the success rates of drug to market launch, higher as well.

Other enabling tools may include:

- Using advanced data analytics and implementing mechanisms for data sharing and interoperability
- Data prioritization
- Integration of alternative data sources, and predictive analytics
- Collaborative partnerships where organizations work together and learn from each other without permanently altering the competitive landscape
- Early payer and patient involvement - a shared set of objectives among regulators, payers and patients earlier that builds trust and engagement among stakeholders.

There are several steps that can be taken to adopt adaptive trial designs, but sometimes finding the advanced expertise can be a challenge in itself. Partnering with a biopharmaceutical services company like PAREXEL on adaptive trial designs helps overcome any existing limitations by providing the skills and resources needed to design, execute and analyze the data from an adaptive trial. They can also offer sponsors the full services that provide statistical expertise for designing these trials, the technology required to collect the data, the support adaptive randomization and provide transparency on dashboards to manage study progress. Further, companies like PAREXEL provide the cross functional study teams for the successful execution, including functions like data management, clinical operations and drug supply and logistics overseen by highly capable Project Managers.

Adaptive trials under new FDA guidelines

PAREXEL's goal in the EIU report was to examine ways to improve the drug development process and make it more efficient, effective and less costly, and more sustainable by using innovations such as adaptive trials. Interestingly, the FDA under the leadership of Scott Gottlieb, MD, has created guidance to encourage the use of adaptive trial designs with clarity on certain requirements for adaptive design planning and implementation. These guidelines that provide the regulatory framework and requirements for the successful implementation of adaptive studies for regulatory approval, signal an opportunity for sponsors to consider adaptive trials when designing their studies.

With the support of the FDA for adaptive trials, there is a greater chance to detect the true effect of a product with a smaller sample size and shorter timeframe, reducing the number of patients unnecessarily exposed to risk. For instance, by including more patients that are more likely to respond positively to the drug and excluding patients more likely to demonstrate an adverse effect, the likelihood of clinical success could be increased.

Conclusion

Given the current unsustainable trajectory of time-to-market, costs and failure rates of drug development, PAREXEL felt the need to address this industry issue by commissioning a study by the EIU to examine how innovations, such as adaptive trials, could drive efficiency and improve success rates and patient outcomes. The report revealed that adaptive trials could enhance the current drug development system by delivering results from a smaller patient population size, recruited in a shorter timeframe, with a higher probability for launch and an increased likelihood of being adopted by payers more quickly.

With the EIU report results and the new FDA guidelines that advocate for adaptive trials, an uptick in the use of greater implementation of these innovative trial designs is expected and with it greater launch success.

Editor's note: In a series on innovations driving drug development of the future, PAREXEL experts recently shared insights on the findings in The Innovation Imperative: The Future of Drug Development pertaining specifically to patient centric clinical trial designs.