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Success divided by effort

Clinical trial productivity on decline, hope for a turnaround

By Brian Orelli, Staff Writer

Despite the strong growth in the number of drugs approved by the FDA over the last few years, clinical trial productivity fell 27% from 2013 to 2018, according to a report from the Iqvia Institute for Human Data Science.

The group devised the Clinical Development Productivity Index that takes into account trial success and effort, which is a combination of the duration of trials and their complexity, including trial size – number of patients, sites and countries – eligibility criteria and endpoints that were gathered from the Clarivate Analytics Cortellis clinical trial database.

"We would say this is not a perfect or ideal index, but it's one that is pragmatic that we can track over time at a therapy area level with a large data sample," Murray Aitken, executive director of the Iqvia Institute, explained on a webcast reviewing the report.

The 27% decline in clinical trial productivity over the last five years has largely come from a 55% decline in productivity for phase I studies. Productivity for phase III studies also declined a little since 2016, although looking further out, phase II and phase III trial productivity has been relatively stable since 2010.

The decrease in productivity for phase I studies was driven by a 35% increase in trial complexity as the average trial duration has increased, although the report notes that the increased time is probably because "more manufacturers are shifting trial design to look for signals of efficacy in earlier stages of development." Oncology was one of the few exceptions, with the average phase I trial time dropping seven months since 2013.

Looking at individual therapy areas for phase I studies, infectious disease, immune, respiratory, neurology, gastrointestinal/nonalcoholic steatohepatitis and endocrinology all experienced decreased productivity. Productivity for phase I oncology and vaccine studies remained stable, while cardiovascular trials increased in productivity.

Improving productivity

While productivity has declined, the institute sees hope for improvement in areas that could drive increased productivity in the coming years. "We think these are eight critical areas to watch because of the magnitude of impact they can bring to clinical trial productivity," Aitken said.

Digital health and mobile technologies are predicted to help increase the use of patient-reported outcomes and experience measures. Wearable electronics can also facilitate the use of biosensors for disease monitoring. And telemedicine can make studies more efficient.

An increase in the use of patient-reported outcomes is expected to decrease the length of studies, especially in the areas of cardiovascular and endocrinology where quality of life is an important aspect of a drug's efficacy. Involving the patient in reporting outcomes can also increase engagement of patients, thereby making the trials run more efficiently.

Productivity may also improve with an increase in the use of real-world evidence, including electronic health records, medical claims data and disease registries to better understand the natural course of a disease, especially in specific populations of patients. In addition to improving trial design, natural history studies can be used to help identify patients and investigators for the study, decreasing recruiting time. The real-world data (RWD) can also be used as comparators for studies in populations where it may be unethical to use a placebo control. "The FDA has also signaled it will additionally accept the use of RWD for initial approvals of new drugs addressing high unmet need," the study notes.

The institute expects that the use of artificial intelligence (AI) to process large datasets will make clinical trials more efficient by building "models to identify desirable characteristics among a set, identify changes that can be made to optimize actions or efficiency, generate new hypotheses, predict future outcomes and inform best decisions." Specifically, the industry experts expect AI to be used to generate new hypotheses that can be tested in studies and to improve study planning and operations, including increasing patient identification and recruitment. Earlier in development, AI should also improve drug discovery, which could increase trial success later.

A continued shift toward targeted therapies should improve productivity through increased success rates in populations with the target. Next-generation therapies, such as cell-based therapies, gene therapies and regenerative medicines, may increase the complexity of studies, but the institute predicts the improved success rates will counteract the increased complexity. Longer follow-ups may be required for therapies that are designed to be cures, but the binary nature of the therapies will allow for quicker successes of pivotal studies using biomarker endpoints.

Changes in the regulatory landscape, driven by the 21st Century Cures Act, the EMA's adaptive pathways approach, the FDA guidance document 21 CFR Part 11 and the EMA's Clinical Trials Regulation, should also have a positive impact on productivity. The regulatory changes will increase the use of novel trial designs and endpoints and decrease regulatory requirements, which should have a positive effect on timelines.

The use of biomarkers should increase clinical trial productivity from picking the right patient population to increasing efficacy signals and reducing side effects. The report notes that it's "difficult to predict the impact of biomarkers on trial duration. While study timelines may decrease due to a higher predicted treatment effect, recruiting narrower patient populations may extend timelines."

Finally, the institute sees clinical trial productivity increasing due to the availability of pre-screened patients and the ability for clinical trial sponsors to recruit patients directly. Access to pools of patients can speed enrollment and decrease screening-failure rates, thereby decreasing clinical trial times.

Of the eight areas highlighted, biomarkers and patient pools are expected to have the greatest impact, increasing productivity over the next five years by 34% and 29%, respectively. Much of the gains will come from expected increases in success rates of 27% and 18%, respectively, but their use is also expected to decrease effort, which improves the overall productivity measurement as well.

AI, regulatory changes, digital health and the use of real-world data are expected to have meaningful improvements on productivity of 12% to 16% over the next five years.

The types of drugs and the use of patient-reported outcomes are expected to contribute a more modest 2% improvement in productivity. In both cases, increases in success rates will be dampened by increases in complexity and timelines that have a negative effect on the productivity index.

We'll know soon enough how well the predictions played out. "Part of our purpose in setting this up and laying this out, including modeling the future, was to enable us to be able to come back to this in a year – or a year or two – and see how have things played out," Aitken said. ♦