MedicalXpress

Number of seamless clinical trials in oncology has risen recently

October 30 2017

The number of early-phase trials in oncology that adopted a seamless approach, as opposed to a traditional trial approach with defined phase I, II, and III plans, is rising, with data from the majority of them presented after 2014, according to a study presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held Oct. 26-30.

"Seamless trials are combined studies where, instead of conducting the conventional phases I, II, and III, the trial adapts and expands based on the results of interim data," said Pedro Barata, MD, MSc, Experimental Therapeutics Fellow at the Cleveland Clinic in Ohio. "First-in-human phase I studies adopting a seamless approach have the flexibility to expand rapidly with multiple cohorts enrolling hundreds of patients in large expansion cohorts, which tends to save time in the drug development process."

The development of more effective therapies and improved patient selection with biomarker discovery in the last decade has led to calls to expedite the drug development process, explained Barata. Consequently, there has been an expansion of creative trial designs that could provide preliminary signals of efficacy and sufficient data to make the tested therapeutics eligible for early approval.

Although seamless design–based early-phase trials are expanding, their prevalence, clinical design, and characteristics are unclear, Barata noted. He and his collaborators conducted a multi-institutional study to evaluate

these factors and their success, by measuring the number of drugs tested in these trials included in the expedited programs run by the U.S. Food and Drug Administration (FDA).

The researchers reviewed all clinical trial abstracts presented at the American Society of Clinical Oncology annual meetings between 2010 and 2017. Seamless trials were defined as any early- phase studies that enrolled 100 or more patients. Of the 1,786 phase I/II trials identified, 3 percent (51 trials) were seamless trials, but accounted for 15 percent of all the patients enrolled. Seamless trials had up to 13 expansion cohorts and data from 65 percent of them were presented after 2014.

Overall, 50 investigational new drugs were tested in early studies using a seamless approach, which included targeted therapies, immunotherapies, antibody-drug conjugates, and chemotherapies, tested as single agents or in combinations.

Data showed that the FDA had granted accelerated approval for eight therapeutics (16 percent) and a priority review for a ninth agent tested in seamless trials. "It is estimated that only 5 percent of oncology drugs that enter human testing ultimately receive FDA approval, therefore, our findings seem to confirm the higher success rate of the drugs studied with the seamless approach," Barata said.

The researchers also found that of the 29 studies published from the 51 seamless trials, 69 percent of them did not have a plan for statistical analysis to calculate the sample sizes of the expansion cohorts.

"Whenever a pre-planned statistical plan is missing, the value of the data is limited, being simply descriptive and demanding further validation," explained Barata. "The numerous, nonrandomized cohorts in each trial and modifications to the study design with multiple amendments put these studies at a higher rate for false-positive or false-negative errors

compared with later-phase trials, thus affecting the validity and interpretation of the data."

While seamless studies offer rapid access to anticancer drugs via accelerated FDA approval, Barata cautioned that concerns, such as potential exposure of patients and drug developers to avoidable risks due to lack of safety monitoring system, communication challenges between pharmaceutical companies, investigators, and regulators regarding frequent protocol modifications, and potential limitations with maintenance of data quality and statistical integrity with these designs need to be addressed in order to improve the quality of this approach and outcomes.

Limitations of the study include its retrospective nature, the inclusion of studies from a single national meeting, and limited access to trial information (meeting abstracts) and not the complete trial protocols.

Provided by American Association for Cancer Research