Providing the Best Possible Cancer Survival Data

Sylvester physician-researcher leads an FDA-AACR-ASA workshop on calculating overall survival in oncology clinical trials.

Lord Kelvin, who invented the temperature scale that bears his name, once said: “If you cannot measure it, you cannot improve it.” Clinical trials are conducted to measure a therapy’s safety and efficacy, but their accuracy hinges on their design. The design of clinical trials is an ongoing discussion among researchers and one that deserves discourse, especially regarding overall survival. While it seems like a simple metric, providing conclusive data on overall survival is rather complex.

To discuss overall survival and the factors that can make accuracy challenging, the U.S. Food and Drug Administration, the American Association of Cancer Researchers (AACR) and the American Statistical Association are partnering to sponsor a workshop, “Overall Survival in Oncology Clinical Trials,” July 18 in North Bethesda, Md.

Ways to Assess Overall Survival

Mikkael Sekeres, M.D., chief of the Division of Hematology at Sylvester Comprehensive Cancer Center and professor of medicine, will chair the workshop’s first session, “Trial Design Considerations for Optimal Assessment of Overall Survival.”

“Determining overall survival – how long somebody lives – is
much more difficult than you might guess,” said Dr. Sekeres, “You would think calculating survival wouldn’t be rocket science, but it turns out that it is.”

What is overall survival? According to the National Cancer Institute, it is the length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive.

In a clinical trial, measuring the overall survival is one way to see how well a new treatment works. In fact, overall survival for cancer patients is a gold-standard endpoint for clinical trials because it measures both efficacy and safety of new therapies. It is also a relatively simple and straightforward metric that matters to patients who want to know if a drug will help them live longer.

Advancements in cancer care have improved the lives of many patients; however, it is becoming increasingly difficult to measure overall survival in a timely fashion to support approval of new drugs that have contributed to the remarkable progress made in the treatment of many cancers. As a result, alternative measures like progression-free survival or durable response rates are being used when submitting drugs to the FDA for approval. In these cases, the FDA often requires companies to provide overall survival data later on, once it becomes available after either accelerated approval or traditional approval. Unfortunately, there are various challenges in monitoring long-term overall survival, such as differences between groups of patients, the design of crossover trials, the treatments patients receive after leaving a trial and changes in the level of benefit compared to the control group.
over time.

In the workshop, stakeholders from across the drug development spectrum will come together to examine the challenges to measuring overall survival in clinical trials and to discuss potential approaches to improve collection and analysis of this important endpoint.

A Complex Problem

Dr. Sekeres has spent years working with the FDA and others to refine clinical studies. For five years, he served on the FDA’s Oncologic Drugs Advisory Committee, the penultimate step before the agency approves a therapy. He is also the senior author on the International Working Group of MDS Clinical Trial Endpoints to define trial goals for myelodysplastic syndrome, a cancerous bone marrow condition that can worsen, becoming acute leukemia.

Clinicians and companies design intricate trials to determine whether a new drug increases survival compared to an old therapy; however, events and other complications can intervene. The COVID-19 pandemic is a good example. How should COVID-19 deaths that occur in patients enrolled into a clinical trial of a drug be counted when measuring overall survival?

“Should we count them, or should we scrub them because they weren’t directly related to the drug?” said Dr. Sekeres. “Or could they have been related to the drug? If it suppressed a person’s immune system, that could have made them more susceptible to COVID. We need to figure out how to deal with these events.”
Better-Designed Trials

Cancers are increasingly defined by their genetic subgroups. In the past, researchers conducted enormous trials for breast, lung, liver and other tumors. But leukemias, for example, have many genetic subtypes, and sometimes these must be attacked differently. As a result, researchers conduct smaller trials, reducing the statistical impact. Dr. Sekeres and colleagues feel that better trial designs could mitigate these complications.

“Maybe we design a trial with a primary endpoint of progression-free survival or duration of response,” said Dr. Sekeres. “But we also set a secondary endpoint to look for improvements in overall survival, because that’s a more meaningful endpoint for patients. In that case, we have to follow patients longer to measure survival.”

The workshop’s ultimate goal is to develop better trials designs that will lead to the approval of important drugs by the FDA. Dr. Sekeres looks forward to a possible FDA white paper, and other guidance, coming out of this event.

“Oncology researchers at Sylvester, and everywhere else, are trying to identify better drugs to treat cancer,” said Dr. Sekeres. “But it’s not enough to develop new therapies. We need to think long and hard about how we test them in patients and work with the FDA and others to ensure clinical trial outcomes truly reflect improved survival.”

For more information about the workshop, visit the AACR’s website.

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