Cancer Organizations Submit Recommendations to Reduce Clinical Trial Barriers

Encourages wider participation of children, people with HIV or hepatitis and those with brain metastasis.

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On August 8, ASCO and Friends of Cancer Research (Friends) submitted to the Food and Drug Administration (FDA) recommended language for five guidance documents on ways to broaden eligibility criteria for cancer clinical trials. The recommendations are part of an ASCO and Friends collaboration to broaden eligibility for participating in clinical trials by addressing five specific areas: minimum age requirements for trial enrollment, HIV/AIDS status, brain metastases, organ dysfunction, and prior and concurrent malignancies.

“Eligibility criteria ensure patient safety, but if they are overly strict, they can jeopardize accrual for clinical trials and reduce the ability to apply trial results to treating patients with cancer in clinical practice,” said ASCO President Monica M. Bertagnolli, MD. “These guidance documents help trial sponsors understand how to modernize eligibility criteria and ensure that trial participants more accurately reflect the patients who will receive a drug after approval.”

Eligibility criteria lay out the characteristics that potential clinical trial participants must meet to participate and often include age, current health status, gender, medical history, and particular type of cancer and its stage. By defining the characteristics of the study population in this way, researchers can better understand the efficacy and toxicity of the study treatment and minimize the impact of confounding factors on interpretation of the study results. However, with more stringent eligibility criteria, fewer patients qualify to participate, making the results less applicable to treat the more diverse patient populations seen in routine clinical practice.

“By reviewing and updating eligibility criteria, significant new opportunities can be given to patients who have historically been excluded,” said Jeff Allen, President & CEO, Friends of Cancer Research. “We commend the FDA and the NCI not only for their willingness to collaborate with external stakeholders to tackle such an important issue, but their commitment to the execution of what will undoubtedly benefit thousands of patients.”

ASCO and Friends launched a collaborative effort in early 2016 to modernize eligibility criteria to

promote greater patient participation in cancer clinical trials. The five areas were identified where eligibility criteria were most likely to restrict a patient's participation in a trial, but least likely to affect the safety of participants. Working groups of researchers, patient advocates, regulators, and industry representatives examined each of the areas and made recommendations on modifying the specific inclusion and exclusion criteria that often restrict participation of patients. ASCO and Friends also worked closely with the FDA throughout the project.

In October 2017, the two organizations published a joint research statement providing a comprehensive examination of eligibility criteria for cancer clinical trials with recommendations to address eligibility criteria in these five specific areas. To help implement these recommendations, ASCO and Friends next drafted guidance documents with rationale and instructions for expanding eligibility criteria in each of these areas:

- Brain metastases: The incidence of brain metastases is increasing in specific cancers, particularly affecting patients with melanoma and cancers of the lung and breast. Excluding patients from clinical trials may mean under representing one-half to one-third of patients with certain types of cancer.
- HIV/AIDS, Hepatitis B, and Hepatitis C: Expanding cancer clinical trial eligibility to be more inclusive of patients with managed HIV, Hepatitis B virus, or Hepatitis C virus infections is justified in most cases and may accelerate the development of effective cancer therapies for patients with these chronic viral infections.
- Minimum age: Greater understanding of the molecular causes of cancer and the similarities of these causes across pediatric and adult cancers provides greater rationale for including children early in oncology clinical trials. Additionally, when clinical trials are undertaken well after extensive testing in adults, potentially promising new therapies are delayed in reaching pediatric patients.
- Organ dysfunction: Patients with organ dysfunction are often excluded from clinical trials, regardless of specific drug metabolism or clearance mechanisms. However, as the general population is aging, there is an increasing number of patients with renal disease, hepatic dysfunction, and cardiac disease who also develop cancer. If a drug does not directly affect particular organs or when organ dysfunction does not directly impact drug metabolism or clearance, patients with lower organ function could participate in a trial. In addition, as data on toxicity become available during drug development, protocols should be revised to include

patients with compromised organ function where safe parameters have been determined.

- Prior and concurrent malignancies: There is an increasing number of patients with prior or concurrent malignancies or comorbidities. By excluding individuals with previous or concurrent cancers or comorbidities, older patients may be prevented from participating.

FDA plans to review the ASCO-Friends recommended language as the agency finalizes draft guidance documents to release for public comment. ASCO and Friends will announce when the draft guidance documents are available for comment and develop comments for submission.

Read the full guidance document submission.

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