ASCO and Friends of Cancer Research Release Comprehensive Recommendations to Broaden Eligibility Criteria for Cancer Clinical Trials

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Alexandria, VA & Washington -- The American Society of Clinical Oncology (ASCO) and Friends of Cancer Research (Friends) are calling for the use of more inclusive eligibility criteria for cancer clinical trials. This recommendation is in conjunction with the release of a Special Series, published today in the Journal of Clinical Oncology (JCO). The series, which includes a joint ASCO-Friends research statement, provides a comprehensive examination of eligibility criteria for cancer clinical trials with recommendations to address eligibility criteria in five specific areas: minimum age requirements for trial enrollment, HIV/AIDS status, brain metastases, organ dysfunction, and prior and concurrent malignancies.

“This joint initiative provides a roadmap for how to safely employ broader eligibility criteria for cancer clinical trials and promote a culture of inclusion,” said ASCO President Bruce E. Johnson, MD, FASCO. “Allowing more patients to participate in clinical trials will ultimately enhance our understanding of how a given treatment should be utilized to treat the diverse patients we see in everyday clinical practice.”

According to the two organizations, eligibility criteria are intended to protect the safety of trial participants — particularly those populations that may be more vulnerable to adverse events.
of a trial drug – as well as define the trial population. Overly restrictive eligibility criteria, however, can impede patient accrual to cancer clinical trials and reduce the generalizability of trial results, making findings more difficult to apply to treatment of real world cancer patients.

“Historically, access to clinical trials has been limited to relatively few patients,” Said Dr. Jeff Allen, President & CEO of Friends of Cancer Research. “Broadening the eligibility criteria for clinical trials will provide the opportunity for more people to participate in research studies. Not only will this improve access, it will make the trial results more reflective of the people that will ultimately use the drug.”

When ASCO and Friends launched the joint project in 2016, 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, comprised 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 U.S. Food and Drug Administration (FDA) throughout the project to address this crucial issue.

The working groups generally found that concerns that have contributed to the historic exclusion of certain groups of patients are often not supported by data. Additionally, since drugs are usually not tested in these specific patient populations until extensive preliminary study has been completed, or after the drug has been approved, arbitrarily excluding these patients limits their access to novel cancer agents and, thus, their ability to benefit from emerging advances in cancer treatment. Moreover, when treating these patients in clinical practice, there is often limited available data on safety and efficacy of drugs for these specific patient populations – patients who may make up a large subset of those with a particular type of cancer.
The Special Series also includes an FDA analysis of Investigational New Drug applications from 2015. Authored by FDA officials, including Director of the FDA's Oncology Center of Excellence Richard Pazdur, MD, the analysis provides further insight into the exclusions of patient populations resulting from common eligibility criteria in cancer trials today, and possible opportunities to broaden eligibility criteria to include more patients in clinical studies.

Building off this effort, ASCO and Friends held a meeting on June 30 to discuss implementation of these broader eligibility criteria with stakeholders across the research community, including 19 drug/biotech manufacturers, FDA, the National Cancer Institute (NCI) Cooperative Groups, and NCI. The organizations will continue to work with clinical trial sponsors and regulators to turn these recommendations into action and identify additional opportunities to safely expand eligibility criteria for oncology trials.

Access the JCO Special Series.

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More detailed information on each recommendation is provided below.

**Recommendations**

**Minimum Age for Enrollment**

*Background:* Cancer patients under the age of 18 have traditionally been excluded from adult clinical trials. In some instances, new treatments for children with cancer may first become available as off-label use after the drug has been approved for adults, and as such, dosing, safety, or efficacy information specific to pediatric use may not be available.

*Recommendations:*

- Pediatric patients should be considered for later-phase trials for cancer types that span both adults and children. Adolescents age 12 and older should routinely be included in these trials because drug metabolism is similar to adults. Inclusion of younger patients may also be appropriate if they are part of the population impacted by the disease, based on the specific biology of the cancer, action of the drug, and available safety information.
- Pediatric patients should be included in early stage trials that assess dosing, safety, and pharmacokinetics when there is scientific rationale to expect that these patients will
benefit and adequate information is available to reduce risk for pediatric participants.

*Read the full article by the minimum age for enrollment working group.*

**HIV**

*Background:* Advances in HIV treatment over recent decades have resulted in normal life expectancy for many individuals with HIV. While cancer is now the leading cause of HIV patient deaths, oncology studies usually exclude patients with HIV from participating.

**Recommendations**

- A patient with HIV who is sufficiently healthy, with low risk of an AIDS-related outcome – as defined by criteria outlined by the authors – should be included in trials for all study phases, particularly for cancers commonly associated with HIV, barring specific rationale for exclusion.
- When enrolled in the trial, patients with HIV should be treated according to the same standards and with the same care as other patients with comorbidities.
- Patients with HIV should be allowed to be treated concurrently with standard antiretroviral therapy while in a cancer trial.

*Read the full article by the HIV working group.*

**Brain Metastases**

*Background:* Patients with brain metastases, even those with stable or treated brain metastases, are often excluded from trials. Exclusion of these patients from participation in trials for cancer types associated with a higher incidence of brain metastases, such as melanoma, breast cancer, and lung cancer, is particularly concerning since they may make up a large portion of the population who will be treated with a drug under development.

**Recommendations:**

- Patients with brain metastases should be regularly included in early drug trials where brain metastases are common in the intended use population.
- Unless there are specific safety concerns or rationale for exclusion, patients should be included in all phases of trials if they have treated and/or stable brain metastases four weeks before entering a study.
- For patients with active brain metastases, there is not a single recommended approach, but these patients should not automatically be excluded from trial participation. The authors provide a decision framework with suggestions and examples for consideration when determining the appropriateness of including these patients based on disease
characteristics, trial design, and investigational agent characteristics.

Read the full article by the brain metastases working group.

Organ Dysfunction

Background: With today's aging population, an increasing number of cancer patients suffer from comorbidities, including renal disease, liver dysfunction, or cardiac disease. Clinical trials often exclude patients with organ dysfunction, however, regardless of the specific mechanism of drug metabolism or clearance.

Recommendations:

- Renal disease: Liberal criteria for creatinine clearance should be used to determine patient inclusion in a trial where renal toxicity is not a direct concern related to the trial therapy and the drug is not eliminated by the kidneys.
- Liver dysfunction: Liver function is not adequately measured with available tests today, however, without alternative measures, enrollment should include standard clinical assessment.
- Cardiac disease: Patients should not be excluded from a trial based on arbitrary ejection fraction values if the investigational drug is not linked to cardiac risks.

Prior or Concurrent Malignancies

Background: With today's aging population, an increasing number of cancer patients have a prior history of cancer or two concurrent cancer diagnoses. Clinical trials often exclude or limit participation for patients with prior or concurrent cancers, even if the other cancer is unlikely to interfere with analysis of the safety or efficacy of the investigational agent against the cancer being treated.

Recommendation:

- Inclusion of patients with prior malignancies is recommended, especially when the risk of the prior malignancy interfering with either safety or efficacy endpoints is very low. Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen should be included.

Read full article by the organ dysfunction and prior or concurrent malignancies working group.

About ASCO:
Founded in 1964, the American Society of Clinical Oncology, Inc. (ASCO®) is committed to making a world of difference in cancer care. As the world's leading organization of its kind, ASCO represents more than 40,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at www.ASCO.org, explore patient education resources at www.Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, and YouTube.

**About Friends of Cancer Research**

Friends of Cancer Research (Friends) drives collaboration among partners from every healthcare sector to power advances in science, policy and regulation that speed lifesaving treatments to patients. For more information, please visit www.focr.org.