

May 13, 2018

Norman Sharpless, M.D.
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Dockets: FDA-2019-D-0357 Brain Mets
FDA-2019-D-0358 Minimum Age for Pediatric Patients
FDA-2019-D-0359 Organ Dysfunction and Prior Malignancies
FDA-2019-D-0363 HIV HCV HBV

Dear Dr. Sharpless,

The undersigned organizations appreciate the opportunity to provide comments on the recently released FDA guidance documents concerning cancer clinical trial eligibility criteria. Clinical trials are the key step in advancing potential new cancer treatments from the research setting to the cancer care clinic, and patient participation in trials is crucial to this success. Most patients express a willingness to participate in clinical research, yet only a small fraction ultimately end up enrolling in a cancer clinical trial due to barriers, such as eligibility criteria, that make participation difficult or even impossible. Consequently, approximately 20% of cancer clinical trials fail due to insufficient patient enrollment, slowing our progress against this disease. For these reasons, we applaud FDA's issuance of these guidance documents, and the clear encouragement to expand eligibility that they represent.

A recent meta-analysis of enrollment barriers to cancer clinical trials found that eligibility criteria on average keep 21.5% of patients from enrolling in clinical trials¹. This represents one of the single largest barriers patients face to enrolling in clinical trials, and therefore deserves careful attention. Eligibility criteria can be necessary to define a scientific question and ensure patient protection, but increasingly criteria do not necessarily serve those purposes and have just propagated from study to study without re-evaluation. A broad group of 17 stakeholders last year endorsed a set of recommendations aimed at reducing barriers to patient enrollment to clinical trials and included in those recommendation was one specific to eligibility criteria².

¹ Unger, J. M., Vaidya, R., Hershman, D. L., Minasian, L. M., & Fleury, M. E. (2019). Systematic Review and Meta-Analysis of the Magnitude of Structural, Clinical, and Physician and Patient Barriers to Cancer Clinical Trial Participation. *JNCI: Journal of the National Cancer Institute*, 111(3), 245–255.
<https://doi.org/10.1093/jnci/djy221>

² Overcoming Barriers to Patient Enrolment in Therapeutic Clinical Trials for Cancer: Recommendations, accessed at: fightcancer.org/clinicaltrialbarriers

Recommendation

Modernize eligibility/inclusion/exclusion criteria to achieve the most relevant parameters that will ensure scientific integrity without unnecessarily excluding patients.

- a) Ensure eligibility criteria do not preferentially exclude a racial or demographic group, e.g. upper age limits, or excluding comorbidities more highly associated with demographic or socioeconomic subgroup unless specific rationale for exclusion exists.*

Listed below are comments on the specific guidance documents.

Brain Metastases

We agree with FDA's guidance encouraging inclusion of patients with brain metastases in clinical trials, when inclusion can be done safely. The suggestion of creating separate cohorts or subset analysis for these patients in early trials provides the opportunity to expand eligibility while isolating any unexpected differences in safety or efficacy.

Patients with HIV, Hepatitis B or Hepatitis C Viral Infections

We agree with FDA's guidance encouraging inclusion of patients with HIV, Hepatitis B or Hepatitis C viral infections. The guidance indicates that any exclusions should be explicitly justified and be based on specific mechanisms of action of the intervention that might pose safety risks based on drug-drug interactions or immune system function.

Minimum Age for Pediatric Patients

Children with cancer are often treated with therapies that have not been thoroughly tested in children and for which no label information regarding safety or dosing for children is available. The challenges that this creates can be partially addressed by greater inclusion of children in clinical trials when doing so can be done safely, ethically and within current regulatory requirements as supported by this guidance. The draft guidance stresses that the inclusion considerations are not only biological, but regulatory as well, given that children are afforded special protections when participating in research. The guidance lays out a rational stepwise framework for research in children and should provide sponsors and institutional review boards greater comfort in designing research that includes children.

Patients with Organ Dysfunction or Prior/Concurrent Malignancies

We support FDA's guidance encouraging inclusion of patients in clinical trials with impaired hepatic and/or renal function when drug pharmacokinetics (PK) and pharmacodynamics (PD) are understood well enough to support safely including such patients in trials. Further, we commend FDA for encouraging inclusion of patients with prior or concurrent malignancies when those conditions are unlikely to affect safety or efficacy assessment of new therapies.

Conclusion

In summary, we are pleased at FDA's interest in encouraging sponsors to safely broaden eligibility criteria, allowing more patients the opportunity to participate in cancer clinical trials. FDA is

encouraging sponsors to provide explicit justification for restrictive eligibility criteria, and once the guidance documents are finalized, we urge FDA to actively challenge sponsors that continue to propose eligibility criteria that are unjustifiably strict.

Thank you again for the opportunity to provide comments, and we look forward to working with you to make sure cancer clinical trials are open to patients who can safely take part in them. If you have any questions, please do not hesitate to contact Mark Fleury (mark.fleury@cancer.org).

Sincerely,

American Cancer Society Cancer Action Network
Association of Community Cancer Centers
Cancer Support Community
Fight Colorectal Cancer
Lazarex Cancer Foundation
Leukemia and Lymphoma Society
LUNGeivity Foundation
Massive Bio
Research Advocacy Network
Signal Path
Susan G. Komen