Cancer Clinical Trial Eligibility Criteria: Available Therapy in Non-Curative Settings

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (OCE) Jennifer Gao at 240-402-4683 or (CDER) Chana Weinstock at 240-402-2625 or (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
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TABLE OF CONTENTS

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I. INTRODUCTION

This guidance provides recommendations to clinical investigators and sponsors regarding the inclusion of patients who have not received available therapy[2] (commonly referred to as existing treatment options) for their cancer in clinical trials of drugs[3] and biological products for the treatment of cancer in the non-curative setting. For the purpose of this guidance, non-curative is generally defined as 1) unresectable, locally advanced, or metastatic disease in solid tumors or 2) hematologic malignancies with unfavorable long-term overall survival.

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II. BACKGROUND

For clinical trials of all products regulated under 21 CFR part 312, including drugs, FDA must determine that study subjects are not exposed to an unreasonable and significant risk of illness or injury (312.42(b)(1)(i) and (b)(2)(i)) to allow such trials to proceed. Therefore, eligibility criteria

[1] This guidance has been prepared by the Oncology Center of Excellence, Center for Drug Evaluation and Research (CDER), and Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] Refer to the guidance for industry *Expedited Programs for Serious Conditions – Drugs and Biologics* (May 2014) for a description of available therapy. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[3] References to drugs include drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262).

should generally require that patients have received available therapy(ies) that offer the potential for cure in a substantial proportion of patients (e.g., available treatment for pediatric acute lymphoblastic leukemia, classic Hodgkin lymphoma, or testicular cancer) in clinical trials evaluating investigational cancer drugs. Alternatively, such available therapy should be administered to all patients in the trial, where the investigational drug is added to such therapy (i.e., add-on trial). However, eligibility criteria in which patients receive an investigational drug(s) in lieu of available therapy is reasonable in the non-curative setting (i.e., when there is no potential for cure or for prolonged/near normal survival) when patients have been provided adequate information to make an informed decision on trial participation.

III. RECOMMENDATIONS

When planning cancer clinical trials in the non-curative setting, sponsors should consider eligibility criteria as it pertains to available therapy. FDA encourages sponsors to discuss their drug development plan with FDA early in development, including their approach to available therapy when developing eligibility criteria. In certain circumstances, FDA may request a specific approach for drug development. When designing cancer clinical trials, the following should be considered in the non-curative setting:

- Expansion of eligibility criteria such that, with appropriate informed consent, patients may be eligible for inclusion in trials of investigational drugs, including first-in-human trials, regardless of whether they have received available therapy in the non-curative setting. In addition to the elements of informed consent required by 21 CFR part 50.25, including "a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject", the informed consent should clearly state that other treatment options known to confer clinical benefit exist, and should include discussion of possible benefits, risks, and uncertainties associated with the drug.[4]

- Evaluation of patients who have received available therapy(ies) and patients who have not in separate cohorts, particularly if interpretation of efficacy results requires a homogenous patient population. Alternatively, analyses of efficacy may be performed in pre-specified subgroup analyses, defined by prior receipt of available therapy(ies).

[4] For additional information on informed consent, see 21 CFR part 50 and the draft guidance for IRBs, clinical investigators, and sponsors *Informed Consent Information Sheet* (July 2014). When final, this guidance will represent the FDA's current thinking on this topic.