4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-0001]

Public Workshop on Minimal Residual Disease; Public Workshop

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop.

SUMMARY: The Food and Drug Administration (FDA), in cosponsorship with the American Society of Clinical Oncology, is announcing a public workshop that will provide a forum for discussion of extending the qualification of minimal residual disease (MRD) detection as a prognostic biomarker to an efficacy/response biomarker in evaluating new drugs for the treatment of acute myeloid leukemia (AML). Our objective is for the workshop to provide a venue for an in-depth discussion of potential endpoints for trials intended to support the approval of new drugs or biologics for treatment of AML. Participants in the workshop will examine if any currently used biomarker can be used as a surrogate endpoint, identify the preferred technology platform and performance characteristics for the assay of the biomarker, discuss any issues regarding ongoing deficiencies in methodological standardization for the biomarker, and determine the need for additional FDA-approved in-vitro diagnostics for AML drug development. The primary focus will be on the biomarkers that are or will soon be ready for incorporation into clinical trials, and the technical and regulatory challenges for use of these markers.

DATES: The public workshop will be held on March 4, 2013, from 8 a.m. to 4 p.m.

ADDRESSES: The public workshop will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Building 31 Conference Center, the Great Room (rm. 1503), Silver Spring, MD

20993-0002. Entrance for the public workshop participants (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information please refer to http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

Complete remission, relapse-free survival, and overall survival are frequently used as endpoints in clinical trials of new therapeutics for AML. These endpoints have some limitations, especially in the context of minimal residual disease. Use of morphological complete remission may miss individuals with clinically significant residual disease who are not truly in remission. For those being followed after remission induction, new evidence of submorphological disease may prompt therapy before morphological relapse. Additionally, for patients with good prognosis, the length of the clinical trial followup may be very long when survival is the

outcome measured, raising logistical and financial challenges for study conduct. More information is needed on whether MRD in AML can be qualified as a response biomarker and then used as a clinical trial endpoint and what the challenges would be to implement use of such an endpoint.

This Public Workshop on Minimal Residual Disease in AML will be one of a series of FDA workshops to establish processes and procedures necessary to qualify a prognostic biomarker, MRD, as a possible response or efficacy biomarker in a group of hematological malignancies. Evaluation of clinical data suggests that MRD can be established as a potential surrogate endpoint for pivotal clinical trials and drug approval given its prominent role as a prognostic indicator in certain subtypes of acute and chronic leukemia. The Office of Hematology and Oncology Products has explored, or plans to explore, the potential utility of MRD as a surrogate endpoint in acute lymphoblastic leukemia (ALL) (including the relapsed setting), chronic lymphocytic leukemia (CLL), and AML. Given the diverse pathophysiology and natural history of these diseases and current practice standards, individualized consideration of MRD as a surrogate endpoint is warranted. The ALL workshop was held on April 18, 2012, and the CLL workshop will be held on February 27, 2013.

II. Structure and Scope of the Workshop

The workshop's scope will include discussions of the use of flow cytometry and molecular methods used to detect and measure minimal residual disease in patients being treated for AML. The workshop will consist of formal presentations examining the regulatory, scientific, and clinical basis for use of biomarkers as potential clinical trial endpoints in AML interspersed with discussions on issues associated with these endpoints.

III. Attendance and Registration

FDA encourages patient advocates, representatives from industry, consumer groups, health care professionals, researchers, and other interested persons to attend this public workshop. There is no registration fee for the public workshop. To register electronically, please use the following Web site: http://www.zoomerang.com/Survey/WEB22GPAXN9NQB (FDA has verified the Web site address, but we are not responsible for any subsequent changes to the Web site after this document publishes in the Federal Register.) Seats are limited and conference space will be filled in the order in which registrations are received. Onsite registration will be available to the extent that space is available on the day of the conference.

Information regarding special accommodations due to a disability, visitor parking, and transportation may be accessed at: http://www.fda.gov/AdvisoryCommittees/default.htm. Under the heading "Resources for You," click on "Public Meetings at the FDA White Oak Campus."

Dated: December 20, 2012.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2012-31043 Filed 12/21/2012 at 4:15 pm; Publication Date: 12/26/2012]