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APPLICATION NUMBER:

214120Orig1s000

OTHER REVIEW(S)

FDA U.S. FOOD & DRUG ADMINISTRATION

Consult Memorandum

Date:	08/17/2020
To:	Emily Jen FDA/OC/CDER/OND/OOD/DHMI
From:	Jacqueline M Cleary CDRH/OPEQ/OHT7/DIHD/IMFB
Through:	Ying Katelin Mao (Branch chief) and Lea Carrington (Division Director)
Subject:	NDA 214120
Drug Name:	Azacitidine
Drug Sponsor	Celgene Corp
Biomarker(s):	Minimal Residual Disease (MRD)
Device Name:	Laboratory Developed Test
Device Sponsor:	(b) (4)
CDRH Tracking Number:	ICC2000416
Related Submissions:	

I. BACKGROUND and PURPOSE

(b) (4)

CDER requested CDRH to review the analytical validity of the assay used to determine MRD.

The clinical trial (NCT01757535) was an international, multicenter, placebo-controlled, Phase 3 study with a double-blind, randomized, parallel-group design which evaluated the safety and efficacy of Azacitidine versus placebo as maintenance therapy in AML patients. Patients were enrolled with de novo acute myelogenous leukemia (AML), AML secondary to prior diagnosis of myelodysplastic syndromes (MDS), or chronic myelomonocytic leukemia (CMML); the patients were aged 55 years or older, and had achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) within 4 months +/- 7 days after intensive induction chemotherapy with or without consolidation therapy. The decision about induction and consolidation therapy regimens was an investigator choice prior to study enrollment. Patients were not candidates for transplant at the time of randomization, which included patients who were not eligible for hematopoietic stem cell transplantation (HSCT), who did not have a transplant donor, or who chose not to proceed to HSCT.

Patients who achieved a CR/CRi after completion of intensive induction therapy with or without consolidation were administered ONUREG 300 mg or placebo orally on Days 1 through 14 of each 28-day cycle. In the event of disease relapse (5% to 15% blasts in peripheral blood or bone marrow), the

dose schedule was extended to 21 days of repeated 28-day treatment cycles. Treatment continued until disease progression (more than 15% blasts were observed in peripheral blood or bone marrow) or until unacceptable toxicity.

Specifically, the CDER seeks advice on:

1. Please assess the analytical validity of the assay used to assess MRD in CC-486-AML-001. The document provided for review of the device is Module 5.3.1.4 (b) (4)

II. BIOMARKER/ANALYTE

(b) (4)

III. DEVICE USE IN THE TRIAL

The assay applied for the analyses has been designed (b) (4)

(b) (4)

3 Pages have been Withheld in Full as B4 (CCI/TS) immediately following this page

(b) (4)

VII. Final Recommendation from CDRH to CDER:

We think it is important to note (b) (4) Many modifications have been made to the original assay that was validated (b) (4) The current version of the assay used in the clinical trial has not been analytically validated. CDRH recommends that the sponsor provide the analytical validation performance data to support the analytical validity of a reliable result being obtained (b) (4) (b) (4) for the MRD measurement in patients with AML in remission as part of the AML 001 study.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

RACHEL S MCMULLEN
08/17/2020 04:50:39 PM

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