

**Food and Drug Administration  
Center for Drug Evaluation and Research**

**Summary Minutes of the Oncologic Drugs Advisory Committee  
March 7, 2018**

Location: FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland.

Topic: The committee discussed supplemental biologic license application (sBLA) 125557/S-013, for BLINCYTO (blinatumomab) injection for intravenous use, application submitted by Amgen, Inc. The proposed indication (use) for this product is for the treatment of minimal residual disease-positive B-cell precursor acute lymphoblastic leukemia.

These summary minutes for the March 7, 2018 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on March 27, 2018.

I certify that I attended the March 7, 2018, meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

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Lauren D. Tesh, PharmD, BCPS  
*Designated Federal Officer, ODAC*

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Bruce J. Roth, MD  
*Chairperson, ODAC*

## Summary Minutes of the Oncologic Drugs Advisory Committee Meeting March 7, 2018

The following is a final report of the Oncologic Drugs Advisory Committee meeting held on March 7, 2018. A verbatim transcript will be available in approximately six weeks, sent to the Division of Hematology Products and posted on the FDA website at:

<https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/ucm597081.htm>

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

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The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on March 7, 2018, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Amgen, Inc. The meeting was called to order by Bruce J. Roth, MD (Chairperson). The conflict of interest statement was read into the record by Lauren D. Tesh, PharmD, BCPS (Designated Federal Officer). There were approximately 150 people in attendance. There was one Open Public Hearing (OPH) speaker presentation.

**Issue:** The committee discussed supplemental biologic license application (sBLA) 125557/S-013, for BLINCYTO (blinatumomab) injection for intravenous use, application submitted by Amgen, Inc. The proposed indication (use) for this product is for the treatment of minimal residual disease-positive B-cell precursor acute lymphoblastic leukemia.

**Attendance:**

**ODAC Members Present (Voting):** Susan Halabi, PhD; Philip C. Hoffman, MD; Grzegorz S. Nowakowski, MD; Vassiliki A. Papadimitrakopoulou, MD; Courtney J. Preusse, MA (Consumer Representative); Bruce J. Roth, MD (Chairperson)

**ODAC Members Not Present (Voting):** Harold J. Burstein, MD, PhD; Heidi D. Klepin, MD, MS; Alberto S. Pappo, MD; Gregory J. Riely, MD, PhD; Brian I. Rini, MD, FACP; Alice T. Shaw, MD, PhD; Thomas S. Uldrick, MD, MS

**ODAC Members Not Present (Non-Voting):** Phuong Khanh (P.K.) Morrow, MD, FACP (Industry Representative)

**Temporary Members (Voting):** Catherine Bollard, MD, FRACP, FRCPA; Andy Chen, MD PhD; Arthur Flatau, PhD (Patient Representative); David Harrington, PhD, MA; Christopher S. Hourigan, DPhil, FACP; Anthony D. Sung, MD

**Acting Industry Representative to the Committee (Non-Voting):** Gary Gordon, MD, PhD

**FDA Participants (Non-Voting):** Richard Pazdur, MD; Ann T. Farrell, MD; Donna Przepiorka, MD, PhD; Emily Jen, MD, PhD; Qing Xu, PhD

**Designated Federal Officer (Non-Voting):** Lauren D. Tesh, PharmD, BCPS

**Open Public Hearing Speakers:** Matthew Zachary (Stupid Cancer)

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*The agenda was as follows:*

Call to Order and Introduction of  
Committee

**Bruce J. Roth, MD**  
Chairperson, ODAC

Conflict of Interest Statement

**Lauren D. Tesh, PharmD, BCPS**  
Designated Federal Officer, ODAC

Opening Remarks

**Donna Przepiorka, MD, PhD**  
Cross-Discipline Team Leader  
Division of Hematology Products (DHP)  
Office of Hematology and Oncology Products (OHOP)  
Office of New Drugs (OND), CDER, FDA

**APPLICANT PRESENTATIONS**

**Amgen, Inc.**

Introduction

**Kathy Kross, MSc**  
Executive Director, Global Regulatory Affairs  
Amgen, Inc.

Overview of MRD+ ALL and Unmet  
Medical Need

**Jerald Radich, MD**  
External Consultant  
Fred Hutchinson Cancer Center

Clinical Efficacy and Safety

**Janet Franklin, MD, MPH**  
Executive Medical Director, Global Development Lead  
for BLINCYTO  
Amgen, Inc.

Benefit-Risk

**Gregory Friberg, MD**  
Vice President, Oncology Global Development  
Amgen, Inc.

A Clinician's Perspective

**Aaron Logan, MD, PhD**  
External Consultant  
University of California, San Francisco

**FDA PRESENTATIONS**

BLA 125557 S013  
Blincyto (blinatumomab)

**Emily Jen, MD, PhD**  
Clinical Reviewer  
DHP, OHOP, OND, CDER, FDA

Statistical Evaluation of Propensity Score  
Analyses

**Qing Xu, PhD**  
Statistical Reviewer  
Division of Biometrics V  
Office of Biostatistics  
Office of Translational Sciences, CDER, FDA

Safety Analysis

**Emily Jen, MD, PhD**

Clarifying Questions

**BREAK**

**OPEN PUBLIC HEARING**

Questions to the Committee/Committee Discussion

**ADJOURNMENT**

***Questions to the Committee:***

1. **DISCUSSION:** Study MT103-203 included patients with MRD  $\geq 0.1\%$ . Do the available data support the cut-off of MRD  $\geq 0.1\%$  as describing a subpopulation of patients with ALL in CR who have a need for pre-emptive therapy?

*Committee Discussion: Members of the committee agreed that patients with MRD  $\geq 0.1\%$  had a very high risk of relapse, but they also noted that the exact population that would benefit from additional therapy is not yet defined. It was also mentioned that patients who are MRD-positive have a higher risk of relapse in general than those considered MRD-negative, but patients with MRD  $< 0.1\%$  might benefit from additional therapy as well, so the agency shouldn't limit treatment to this level as the scientific assays are constantly improving with time and the ability to detect MRD at lower concentrations in the future might arise. It was also brought up that the scientific community does not yet know if the eradication of MRD improves long-term clinical outcomes and that randomized controlled trials are needed. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Do the results of MT103-203 demonstrate that for patients with ALL in CR who have MRD  $\geq 0.1\%$ , treatment with blinatumomab provides a potential benefit that outweighs the risks from the treatment?

**Vote Result:      Yes: 8              No: 4              Abstain: 0**

**Committee Discussion:** *Eight committee members voted “Yes” that the results of MT103-203 demonstrate that for patients with ALL in CR who have MRD  $\geq$  0.1%, treatment with blinatumomab provides a potential benefit that outweighs the risks from the treatment. Four members voted “No”. It was mentioned that it is not clear where blinatumomab would be used in the treatment cascade given that based on the data presented a “potential” benefit was assumed from trends in the data, but 80% of the patients went to transplantation so the benefit with receiving blinatumomab is confounded. Comments were made about seeing clinical trials conducted for blinatumomab versus transplantation alone and more data on patients who get blinatumomab who convert to MRD negative status who then go on to get transplantation and their long term outcomes. One of the members who voted “No” mentioned that the clinical data looks promising, but it is not a strong enough clinical conclusion to merit FDA labeling for this indication. One member noted that they would like to have the option of blinatumomab available for patients who aren’t able to go on to transplantation but might benefit from being MRD negative. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 11:45 a.m.