

Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
October 10, 2018

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

Topic: The committee discussed biologics license application 761088 for CT-P10, a proposed biosimilar to Genentech, Inc.'s RITUXAN (rituximab), submitted by Celltrion, Inc. The proposed indications (uses) for this product are for the treatment of adult patients with (1) relapsed or refractory, low-grade or follicular, CD20-positive, B-cell Non-Hodgkin's Lymphoma (NHL) as a single agent; (2) previously untreated follicular, CD20-positive, B-cell NHL in combination with first-line chemotherapy and, in patients achieving a complete or partial response to CT-P10 in combination with chemotherapy, as single-agent maintenance therapy; and (3) non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone.

These summary minutes for the October 10, 2018 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on November 5, 2018.

I certify that I attended the October 10, 2018 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/
Lauren D. Tesh, PharmD, BCPS
Designated Federal Officer
ODAC

/S/
Brian I. Rini, MD, FACP
Chairperson
ODAC

**Final Summary Minutes of the
Oncologic Drugs Advisory Committee (ODAC) Meeting
October 10, 2018**

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on October 10, 2018, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Celltrion, Inc. The meeting was called to order by Brian I. Rini, MD, FACP (Chairperson). The conflict of interest statement was read into the record by Lauren D. Tesh, PharmD, BCPS (Designated Federal Officer). There were approximately 175 people in attendance. There were five Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The meeting focused on discussion of biologics license application (BLA) 761088 for CT-P10, a proposed biosimilar to Genentech, Inc.'s RITUXAN (rituximab), submitted by Celltrion, Inc. The proposed indications for CT-P10 are: treatment of adult patients with (1) relapsed or refractory, low-grade or follicular, CD20-positive, B-cell Non-Hodgkin's Lymphoma (NHL) as a single agent; (2) previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy, and (3) non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy.

Attendance:

Oncologic Drugs Advisory Committee Members Present (Voting): Massimo Cristofanilli, MD, FACP; Susan Halabi, PhD; Christian S. Hinrichs, MD; Heidi Klepin, MD; Grzegorz S. Nowakowski, MD; Brian I. Rini, MD, FACP (Chairperson); Thomas S. Uldrick, MD, MS

Oncologic Drugs Advisory Committee Members Not Present (Voting): Philip C. Hoffman, MD; Vassiliki A. Papadimitrakopoulou, MD; Alberto S. Pappo, MD; Courtney J. Preusse, MA (Consumer Representative); Gregory J. Riely, MD, PhD; Alice T. Shaw, MD, PhD

Oncologic Drugs Advisory Committee Members Present (Non-Voting): Phuong Khanh (P.K.) Morrow, MD, FACP (Industry Representative)

Temporary Members (Voting): Andy L. Chen, MD, PhD; Jerry M. Collins, PhD; William S. Hancock, PhD; Randy Hawkins, MD (Acting Consumer Representative); Adel H. Karara, PhD, FCP; Eric O. Long, PhD; Tracy G. Matson (Patient Representative); Paul J. Smith, PhD, MS; Scott A. Waldman, MD, PhD

FDA Participants (Non-Voting): Ann Farrell, MD; Sue Lim, MD; Nicole Gormley, MD; Steven Kozlowski, MD; Vishal Bhatnagar, MD; Christopher Downey, PhD

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

Open Public Hearing Speakers: Jim Koeller, MS; Sonia T. Oskouei, PharmD, DPLA; Kashyap Patel, MD; Susannah Koontz, PharmD, BCOP, FHOPA; Joseph P. Fuhr, Jr., PhD

The agenda was as follows:

Call to Order and Introduction of Committee

Brian I. Rini, MD, FACP
Chairperson, ODAC

Conflict of Interest Statement

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

Opening Remarks

Vishal Bhatnagar, MD
Medical Officer Team Leader (Acting)
Division of Hematology Products (DHP)
Office of Hematology and Oncology Products (OHOP)
Office of New Drugs (OND), CDER, FDA

APPLICANT PRESENTATIONS

Analytical Biosimilarity and Nonclinical Assessment

Celltrion, Inc.

Elizabeth Pollitt, PhD
CMC Expert, BPCRCS Ltd
Former Vice President CELLTRION, Inc.

Clinical Pharmacology, Efficacy and Safety Assessment

Alexey Kudrin, MD, PhD, MBA
Clinical Expert, Biotech Consultancy Services Ltd
Former Vice President CELLTRION, Inc.

Clinical Perspective

David Alan Rizzieri, MD
Professor of Medicine
Chief, Section of Hematologic Malignancies
Associate Director for Clinical Research
Division of Hematologic Malignancies and Cellular Therapy
Duke Cancer Institute, Duke University School of Medicine

FDA PRESENTATIONS

Product Quality

Haoheng Yan, MD, PhD
Product Quality Reviewer
Division of Biotechnology Review and Research IV
Office of Biotechnology Products
Office of Pharmaceutical Quality, CDER, FDA

Yu-Ting Weng, PhD
Product Quality Statistical Reviewer
Division of Biometrics VI
Office of Biostatistics (OB)
Office of Translational Science (OTS)
CDER, FDA

Clinical Pharmacology and Immunogenicity Assessment

Sang M. Chung, PhD
Clinical Pharmacology Reviewer

Division of Clinical Pharmacology II
Office of Clinical Pharmacology
OTS, CDER, FDA

Clinical Efficacy and Safety

Rachel Ershler, MD
Clinical Reviewer
DHP, OHOP, OND, CDER, FDA

Clarifying Questions to Presenters

Cindy Gao, PhD
Clinical Statistical Reviewer
Division of Biometrics V
OB, OTS, CDER, FDA

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. DISCUSSION: Please discuss whether the evidence supports a demonstration that CT-P10 is highly similar to US-licensed Rituxan, notwithstanding minor differences in clinically inactive components.

Committee Discussion: *The committee was in consensus that the totality of evidence based on various analytical, in-vitro, biological, and pharmacokinetic/pharmacodynamic testing, with orthogonal results filling information gaps, demonstrates robust evidence of high similarity between US-licensed Rituxan and CT-P10. Some members found the explanation of minor structural differences not affecting critical biological activities as beneficial because molecular biology translates well into in-vitro studies, indicating similarity. Please see the transcript for details of the committee discussion.*

2. DISCUSSION: Please discuss whether the evidence supports a demonstration that there are no clinically meaningful differences between CT-P10 and US-licensed Rituxan.

Committee Discussion: *The committee was in consensus that the clinical trials presented no evidence to suggest a clinically meaningful difference between US-licensed Rituxan and CT-P10. The panel took into consideration the complimentary design of the non-inferiority trial, the explanation of the adverse events, and the prespecified margins, agreeing none showed significant differences. One member stated that the neutropenia safety signal was adequately explained. Please see the transcript for details of the committee discussion.*

3. DISCUSSION: Please discuss whether there is adequate justification to support licensure for the proposed indications sought by the Applicant.

Committee Discussion: *The committee was in consensus that all three proposed indications are consistent with current use, and the evidence presented supports each indication adequately. Please see the transcript for details of the committee discussion.*

4. **VOTE:** Does the totality of the evidence support licensure of CT-P10 as a biosimilar product to US-licensed Rituxan for the following indications:

Treatment of adult patients with

- a. relapsed or refractory, low-grade or follicular, CD20-positive, B-cell Non-Hodgkin's Lymphoma (NHL) as a single agent
- b. previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
- c. non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy.

Vote Result: **YES: 16** **NO: 0** **ABSTAIN: 0**

Committee Discussion: *The committee unanimously agreed that the totality of analytical, pharmacologic, immunogenicity, and clinical evidence supported the licensure of CT-P10 for all three proposed indications based on the high degree of similarity, except for minor components, between US-licensed Rituxan and CT-P10. Some members mentioned the possible benefit to access for patients as well as price reduction to the healthcare systems post-approval. One member indicated the safety signal as a concern, but considered the lower number of patients treated as a possible reason for the imbalance. One member stated that the molecular discrepancies identified in analysis were overwhelmed by the clinical results. Please see the transcript for details of the committee discussion.*

The meeting on October 10, 2018 was adjourned at approximately 11:35 a.m.