Waiver to Allow Participation in a Food and Drug Administration Advisory Committee

DATE: December 30, 2022

TO: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

FROM: Byron Marshall
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Meeting Temporary Member: **Kristen Ciombor, M.D., MSCI**

Committee: Oncologic Drugs Advisory Committee

Meeting date: February 9, 2023

Description of the Particular Matter to Which the Waiver Applies:

Dr. Kristen Ciombor is a temporary voting member of the Oncologic Drugs Advisory Committee. The committee's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cancer and make appropriate recommendations to the Commissioner of Food and Drugs.

On February 9, 2023, the committee will discuss investigational new drug application (IND) 157775, for dostarlimab-gxly for injection, submitted by GlaxoSmithKline LLC. The proposed indication (use) for this product is as a single agent for the treatment of patients with locally advanced, treatment-naïve mismatch repair deficiency/microsatellite instability-high rectal cancer. FDA would like to obtain the committee's input on the following: (1) the adequacy of the proposed trial(s) to evaluate the benefits and risks of dostarlimab for the proposed indication, including trial design, study population, clinical endpoint, and patient follow-up; and (2) the adequacy of the proposed data package to permit an assessment of the benefits and risks of dostarlimab for the proposed indication. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Ciombor's employer, Vanderbilt University, is participating in a study titled *A Phase II Study of Neoadjuvant Nivolumab Plus Ipilimumab and Short-Course Radiation in MSI-H/dMMR Locally Advanced Rectal Adenocarcinoma (NCT04751370)*, sponsored by the National Cancer Institute, an unaffected entity. The study protocol is in the process of being amended in which the study population will overlap with the indication coming before the advisory committee. The study began on May 13, 2021, with an anticipated end date of (b) (4). Vanderbilt University anticipates receiving a total between $0 and $8,000 per patient enrolled in the study. At the writing of the waiver, Vanderbilt has accrued (b) (4) to this trial. Dr. Ciombor serves as National Principal Investigator of the study and she does not receive any salary support from the study funding.

Basis for Granting the Waiver:

Dr. Kristen Ciombor has unique qualifications and specialized expertise needed for this particular matter.

Dr. Ciombor is Associate Professor in the Division of Hematology/Oncology within the Department of Medicine at the Vanderbilt University School of Medicine in Nashville, Tennessee. She is a Staff Physician at the Vanderbilt University Medical Center, and Member of the Vanderbilt-Ingram Cancer Center.

Dr. Ciombor received her bachelor's degree in biochemical sciences from Harvard University and her medical degree from the University of Miami Miller School of Medicine in Miami, Florida. She completed her internal medicine residency and chief residency at the University of Miami/Jackson Medical Center/Miami Veterans Affairs Medical Center. She then completed her fellowship in hematology/oncology at Vanderbilt, where she also graduated with a Master of Science in Clinical Investigation.

Prior to joining the Vanderbilt faculty in 2017, Dr. Ciombor was Assistant Professor of Internal Medicine, Division of Medical Oncology at the Ohio State University. A board-certified medical oncologist, Dr. Ciombor specializes in the treatment of patients with gastrointestinal (GI) cancers. Her research involves the design and implementation of clinical trials for GI malignancies, particularly colorectal cancer. She also has a research interest in translational medicine for the development of prognostic and predictive biomarkers and in better understanding of genomics in colorectal cancer.

The particular matter is not sensitive.

This meeting topic is not considered to be sensitive as the FDA Division responsible for review of this product does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial.

Dr. Kristen Ciombor's expertise in this particular matter is necessary in the interest of public health.

Colorectal carcinoma (CRC) is the second leading cause of cancer-related deaths in the United States, with an estimated 151,030 cases of CRC and an estimated 52,580 deaths in 2022. In 2019, there were an estimated 1,369,005 people living with colorectal cancer in the United States. Rectal cancer accounts for approximately one-third of newly diagnosed cases of CRC. Mismatch repair deficient or microsatellite instability high (dMMR/MSI-H) CRC accounts for approximately 5-10% of cases.

Locally advanced rectal cancers (LARC) are tumors originating within the rectum that are clinical stage II or III (T3-4 and/or node-positive) as defined by pelvic magnetic resonance imaging or endoscopic ultrasound. A comprehensive trimodality approach involving neoadjuvant chemoradiotherapy, total mesorectal excision, and systemic chemotherapy has been the standard of care in the US for most medically operable patients with nonmetastatic, locally advanced rectal cancer. Standard of care is curative for most patients, but it is associated with treatment-related morbidity, including need for colostomy following surgery and long-term radiation-related adverse events (e.g., bowel and bladder dysfunction). There is growing interest in non-operative treatment options to avoid surgical morbidity and improve quality of care for patients. However, non-operative management approaches are not standard and there are limited data to support broad use of trial designs, clinical trial endpoints, guidelines for selecting and monitoring patients for studies evaluating systemic therapies indicated for the treatment of LARC.

In the interest of public health, it is important that the Agency has available the expertise that Dr. Ciombor will provide for the discussion of the particular matter before the committee.

Any potential for a conflict of interest is greatly outweighed by the strong need for Dr. Kristen Ciombor's expertise in this matter.

The FDA would like to obtain the committee's input on the adequacy of the proposed trial(s) to generate the data that will facilitate an evaluation of the benefits and risks of dostarlimab for the proposed indication, including trial design, study population, clinical endpoint, and patient follow-up.

Dr. Ciombor's professional experiences as a medical oncologist with expertise in the treatment of rectal cancer combined with her research experiences will be invaluable to a robust and productive discussion on the issue coming before the committee.

Accordingly, I recommend that you grant Dr. Kristen Ciombor, a temporary voting member of the Oncologic Drugs Advisory Committee, a waiver from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

✓ The individual may participate, pursuant to 18 U.S.C. 208(b)(3) – The need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved.

Limitations on the Regular Government Employee's or Special Government Employee's Ability to Act:

_____ Non-voting

_____ Other (specify):

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_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S
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Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

January 24, 2023
Date