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March 11, 2021

Steven D. Pearson, MD, MSc
President
Institute for Clinical and Economic Review (ICER)
Two Liberty Square
Boston, MA 02109

Re: ICER's Assessment of Treatments for Multiple Myeloma

Dr. Pearson,

The American Society of Hematology (ASH) appreciates the opportunity to offer comments in response to the Institute for Clinical and Economic Review's (ICER) Draft Evidence Report: Anti B-Cell Maturation Antigen CAR T-cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma.

ASH represents more than 17,000 clinicians and scientists worldwide who are committed to the study and treatment of blood and blood-related diseases. These disorders encompass malignant hematologic disorders such as leukemia, lymphoma, and multiple myeloma, as well as non-malignant conditions such as sickle cell disease, thalassemia, bone marrow failure, venous thromboembolism, and hemophilia. In addition, hematologists are pioneers in demonstrating the potential of treating various hematologic diseases and continue to be innovators in the field of stem cell biology, regenerative medicine, transfusion medicine, and gene therapy.

ASH has two general concerns about ICER's draft evidence report, which assesses the clinical effectiveness and value of three treatments for multiple myeloma, idecabtagene vicleucel, ciltacabtagene autoleucel, and belantamab mafodotin. First, ASH believes that this analysis and any comparisons of these agents are premature, since there is not yet a significant patient population treated at recommended doses to fairly assess response rates, as well as median progression free survival (PFS) and overall survival (OS). Ultimately, there have been too few patients treated and limited time for follow-up for this analysis to be meaningful at this time. Second, while ASH appreciates the need to make data-driven policies, it is difficult to quantify the "value" assigned to human suffering and the ability of a highly effective therapeutic agent to reduce the distress and suffering experienced by an ineffectively served subset of myeloma patients. While the Society appreciates the discussion in the "Contextual Considerations" chapter about the more difficult to quantify elements, ultimately these considerations are not included in the ICER's modeling in the Draft Evidence Report so they have less utility and impact.

ASH's specific concerns with this review are outlined below.

Challenges Unique to the Multiple Myeloma Population

The Society believes that there are challenges unique to the multiple myeloma (MM) model. For example, unlike the non-Hodgkin's lymphoma (NHL) population that was used as a benchmark for the NHL assessment on chimeric antigen receptor (CAR) T-cells, the population of MM patients is more biologically diverse. This makes it much harder to make the one-to-one comparisons between different therapeutic approaches. In the domain of

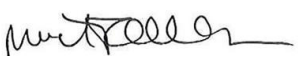
NHL, there is also less diversity of third- and fourth-line therapeutic regimens than there is in the domain of MM patients. Moreover, there are no real sixth line therapies for the NHL population while there are for patients with MM. This vastly complicates the economic modeling involved in estimating the differential cost between the "standard" approach and the three novel approaches that were the focus of this report. In addition, absence of a more rigorous risk segmentation model further limits the ability to adequately economically model out clearly risk-segmented populations for a reproducible "apples to apples" comparison.

Additional Comments

- The relationship between PFS and OS for belantamab mafodotin needs further study, as does the definition of the dose which can minimize keratopathy and decrease modifications in planned treatment, as occurs at present.
- Nothing is included regarding minimal residual disease responses in all three therapies and its implications.
- Finally, patients with MM and their caregivers have the challenge of ophthalmologic evaluation – an additional time and cost burden – before each visit, which needs to be included in analysis.

Thank you for the opportunity to submit comments. Should you have any questions or if you would like to discuss these comments further, please reach out to Leslie Brady, ASH Policy and Practice Manager, at lbrady@hematology.org or 716-361-2764 (cell).

Sincerely,



Martin S. Tallman, MD
President