



# AMERICAN SOCIETY OF HEMATOLOGY

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## 2024

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Robert M. Califf, MD  
Commissioner  
U.S. Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

Re: *Docket No. FDA-2024-N-0018 for "Oncologic Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket."*

Dear Commissioner Califf:

The American Society of Hematology (ASH) is pleased that the U.S. Food and Drug Administration (FDA) is taking important steps to evaluate and respond to the recently discovered secondary malignancies following treatment with CAR T-cell therapies. This includes review of T cell malignancy risk and other topics related to the safety and efficacy of these therapies at the March 15th Oncologic Drugs Advisory Committee (ODAC) meeting with the sponsors of the related therapies. ASH appreciates the opportunity to submit the following comments as part of the public comment docket (FDA-2024-N-0018) for the March 15th ODAC Meeting. ASH's feedback is not specific to the therapies being evaluated but includes important considerations for the Agency related to adverse events associated with all CAR-T therapies.

ASH represents more than 18,000 clinicians and scientists worldwide committed to studying and treating 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 fields of stem cell biology, regenerative medicine, gene therapy, transplantation, and transfusion medicine. ASH membership is comprised of basic, translational, and clinical scientists, as well as physicians providing care to patients. The content of this letter includes feedback from ASH members with expertise in hematologic malignancies and secondary malignancies.

In 2018, ASH founded the ASH Research Collaborative (ASH RC) to accelerate change by making it more efficient to conduct research, from increasing access to high-quality clinical data to making it easier for individuals with hematologic conditions to participate in studies. Current ASH RC initiatives focus on multiple myeloma and sickle cell disease (SCD). The foundation of the ASH RC is its Data Hub, which is a shared data resource for the global hematology community -- a resource for industry, the FDA, and others to efficiently collect real world and prospective post-approval cell and gene therapy product data, specifically for multiple myeloma and SCD. This real-world data can generate actionable insights for research, regulatory needs, and quality improvement.

### *Long-Term Follow-up for Innovative Therapies is Essential*

Expanding approaches and applications of gene and cell therapies for hematologic diseases is a major ASH priority. ASH is excited to see the rapid advances in gene and cellular therapies and the promising new therapeutic options that continue to change care for individuals with

hematologic conditions. Additionally, the Society has a significant interest in the safety and efficacy of cell and gene therapy products. As we have recently seen with the secondary cancer risk tied to CAR-T therapies, the long-term follow-up of individuals who undergo these treatments continues to be critical to ensure the best outcomes for those patients and to help inform the research and use of these therapies over time. We were pleased to [respond to the FDA's 2023 call for input on methods and approaches for capturing post approval data for these products](#). As noted in this letter, ASH and the ASH Data Hub continue to lead efforts to support the advancement and long-term follow-up of these therapies, and we hope the FDA will leverage the Society's resources and expertise as the Agency continues to consider data collection for these transformative therapies. ASH is pleased that the Center for International Blood and Marrow Transplant Research (CIBMTR) and the FDA Adverse Events Reporting System (FAERS) are collecting and assessing critical information about the long-term issues related to many of these therapies. The ASH RC is having discussions with CIBMTR to explore projects that would expand beyond data collection to be linked with real world data (RWD) through the ASH RC Data Hub, such as electronic health record data that also incorporates data validation.

### ***Importance of Comprehensive Communication and Educations about Gene and Cell Therapies***

ASH would like to highlight the importance of thoughtful, measured, and comprehensive communication and education about the potential risks and benefits of these therapies. The messaging around this issue could have a significant impact on patients currently receiving CAR-T therapy or those considering this treatment modality and could affect future research on treatment of other diseases with CAR-T therapy. We were pleased that the FDA has repeatedly acknowledged that the overall benefits of CAR T-cell treatment outweigh their potential risks, and it will be important to continue to make sure those risks are placed in the context of therapies administered prior to cellular therapies, which also may be associated with secondary malignancies. We welcome the opportunity to work with the Agency as you continue to frame messaging about this issue moving forward. Additionally, it is imperative that providers are continuously reminded about the importance of long-term follow-up and reporting these toxicities; aware of the type of testing that is needed to accurately identify the underlying cause for the onset of the secondary malignancy; and updated on how to most effectively manage patients with these secondary malignancies. ASH will continue to engage with the Agency as the Society identifies ways to communicate these essential messages.

### ***ASH Convening Key Stakeholders to Collectively Address Toxicity Issues Related to Immunotherapies***

Finally, ASH is exploring the possibility of convening other medical and scientific organizations and established registries in the cell and gene therapy space to discuss ways in which collectively we can advance the following as it relates to secondary malignancies resulting from CAR-T therapies:

- Fostering scientific exchange to understand the biology surrounding the onset of these secondary malignancies;
- Facilitating the reporting of these toxicities;
- Developing educational resources on management approaches for these toxicities; and
- Informing policy changes related to these toxicities.


We will keep the FDA apprised of this effort as we think it would be valuable to have representation from the Agency as appropriate.

ASH appreciates the opportunity to provide these comments. Please consider ASH a resource; we would be pleased to provide additional information. If you have any questions, please use ASH Deputy Director of Government Relations and Public Health Stephanie Kaplan ([skaplan@hematology.org](mailto:skaplan@hematology.org) or 202-776-0544) as your point of contact.

Sincerely,



Mohandas Narla, DSc  
President



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