American Society for Blood and Marrow Transplantation
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Centers for Medicare and Medicaid Services
Center for Clinical Standards and Quality
Coverage and Analysis Group
S3-02-01, 7500 Security Boulevard, Baltimore, MD 21244
Via email to: MedCACpresentations@cms.hhs.gov
CC: Maria Ellis, Executive Secretary for MEDCAC, Maria.Ellis@cms.hhs.gov

RE: MEDCAC Meeting, CAR-T

The American Society for Blood and Marrow Transplantation (ASBMT) is a professional membership association of more than 2,200 physicians, scientists and other healthcare professionals promoting blood and marrow transplantation and cellular therapy through research, education, scholarly publication and clinical standards. The ASBMT is dedicated to improving the application and success of hematopoietic cell transplants (HCT) and other cellular therapies. To that end, we respectfully submit the following commentary regarding the planned discussion of Patient Reported Outcomes (PROs) in the context of Chimeric Antigen Receptor T cell therapy (CAR-T) at the August 22 MEDCAC meeting.

In Federal Register notice CMS-3363-N, CMS notes that it is

> *seeking the MEDCAC's recommendations regarding collection of patient reported outcomes (PRO) in cancer clinical studies. The MEDCAC will specifically focus on appraisal of evidence-based PRO assessments to provide information that impacts patients, their providers, and caregivers after a CAR T cell therapy intervention for the patient's cancer.*

The ASBMT identified 20 members as experts in the areas of PROs and HCT/CAR-T. In the weeks after CMS' announcement, a subgroup was convened to discuss CMS' charge to MEDCAC over the course of several calls. The ASBMT understands the Agency's interest in PROs and supports the collection of PROs throughout healthcare, and particularly in oncology. H**owever, the ASBMT strongly objects to any mechanism that would tie patient access or provider reimbursement to the reporting of PROs, especially in the case of CAR-T therapy.** There are several factors that make mandated reporting of PROs, through the Coverage with Evidence Development (CED) mechanism or otherwise, problematic at the current time. A summary of key issues follows.

Challenges with Conducting PRO Studies in the CAR-T Treatment Population

- **Optimal instruments, measurements and timepoints are currently unknown**. The currently available PRO measures were developed in the era of chemotherapy; the relevant and important PROs for immunotherapies, particularly CAR-T, are not yet identified. Due to the type and severity of toxicities associated with CAR-T, measurement during the presence of Cytokine Release Syndrome (CRS) and/or neurotoxicity may not be possible. *Mandating the use of a current instrument or set of outcomes through NCD or CED will set a course of collecting data that is very likely to be inaccurate and inadequate.*

- **Feasibility of PRO studies for CAR-T on a wide-scale basis is not currently well understood.** Aside from the logistical challenges associated with new data collection (building instruments into electronic forms), there will be the need for on-going outreach when patients leave the treatment center. Specific long-term follow-up data collection and analysis concerns include relapse, understanding the impact of co-morbidities and secondary malignancies, and analyzing PROs in the context of subsequent exposure to other treatments, such as HCT. *Finally, not all centers are capable of quickly launching and supporting high-quality PRO studies, which would create significant gaps in access if PROs become part of a National Coverage Determination or CED mechanism.*

- **There is significant heterogeneity in the CAR-T constructs and the associated disease indications.** The aforementioned concerns will be multiplied as CAR-T products diversify and as more indications are approved. The PROs and instruments deemed appropriate for patients receiving CAR-T for pediatric B-cell Acute Lymphomblastic Leukemia may be very different from those appropriate for assessing patients with Diffuse Large B-cell Lymphoma; each of these could again be very different from PROs for myeloma patients. *Products will utilize different scientific constructs and the timeframes for clinical response and/or potential onset of toxicities may differ for each construct, which will challenge the establishment of set timepoints for data collection.*

CAR-T PRO Working Group

The ASBMT member experts that participated in this discussion process have suggested that CMS participate in a multi-institutional working group currently being formed to study the use of PROs in CAR-T patients. The working group intends to do the following: 1) formalize a multi-institution collaboration, 2) harmonize patient-level data from existing studies to increase statistical power and identify PRO measures most sensitive to change, 3) conduct pilot studies across several institutions to assess feasibility, evaluate the performance of PRO instruments and assess the need for CAR-T specific instruments, 4) develop consensus on outcomes that should be assessed and which PRO instruments are best suited to measure them, and 4) develop strategies for routine assessment of PROs alongside appropriate real-time interventions.

We would welcome the Agency's participation in this working group. If you have any questions or require additional information, please contact Stephanie Farnia at SFarnia@asbmt.org.

Sincerely,

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