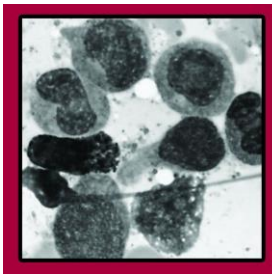

ASBMT™
American Society for Blood and Marrow Transplantation

Executive Office
85 W. Algonquin Road, Suite 550
Arlington Heights, IL 60005-4460

Telephone: (847) 427-0224
Fax: (847) 427-9656
Email: mail@asbmt.org
Web: www.asbmt.org

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

January 23, 2018

Dr. Pearson:

The American Society for Blood and Marrow Transplantation (ASBMT) appreciates the opportunity to comment on the Institute for Clinical and Economic Review's draft evidence report on Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value. The 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 and other cellular therapies, such as CAR-T.

Hematopoietic cell transplantation (HCT), also known as stem cell transplantation (SCT), is a medical sub-specialty comprised of physicians with Board Certifications in Internal Medicine, Medical Oncology, Pediatrics, Hematology and/or Immunology. Due to their unique clinical expertise and training, ASBMT member clinicians and cellular therapy programs will be the primary individuals and teams initially providing CAR-T to patients in need of treatment. We anticipate that CAR-T is the first of many engineered cellular therapies to be approved in the coming decade.

In our prior comments to ICER regarding the Draft Scoping Document, we noted that both the clinical and financial data are immature for this type of analysis. **We maintain the position that an evaluation of CAR-T is premature at this time.** As both approved products have only been indicated for use by the U.S. Food and Drug Administration for less than six months, our knowledge of the patients receiving CAR-T is largely limited to the small population treated while on clinical trial. We expect that the populations receiving treatment from this point forward will be more clinically heterogeneous than while on the trial. The clinical heterogeneity of the new treatment population will be dwarfed by the financial heterogeneity associated with their treatment, as cell therapy programs are still learning how to integrate the cost of the product into the financial process and how to track the costs of care. Currently, there are not accurate,

consistent and comprehensive diagnosis or procedure codes available between care settings, thus it is not yet possible to conduct multi-center, multi-payer assessments of the average costs of care.

Given that we understand ICER's intention is to move forward with the analysis, we offer the following specific comments on the draft evidence report.

1) We acknowledge and support ICER's inclusion of patient and family perspectives in the report. The physical, emotional and financial burden on the patients and families of those being treated for these disease should continue to be a focal point in these types of analyses.

2) **The assumed $100,000 mark-ups on CAR-T products is not a well-substantiated number and should be removed from the analysis or decreased substantially**. There are numerous issues associated with the estimated mark-ups being utilized for either product in the report. First, we note that the term 'mark-up' in the ICER report appears to represent a realized (i.e. reimbursed) margin paid to the provider at the time of claim adjudication. Mark-up generally refers to practice of adding overhead facility costs to the acquisition cost of a product to create the amount placed on a claim, known as the charge, which is then sent to a payer. Claims are then adjusted based on contracts and negotiated rates and a payment is sent to the provider. Thus, the initially filed mark-up is often vastly different than the payment received by the facility. For purposes of this comment, we will interpret ICER's references to mark-up as representing a *paid mark-up* to the provider, vs. what the provider may have filed as a charge on a claim.

   On page 45, the authors note that "Most stakeholders with hospital billing expertise agreed that CAR-T mark-ups will be varied and may not follow the relative multiplier norms for other hospital administered therapies." *This sentiment cannot be overstated; CAR-T does not follow the typical mark-up practices due to the high price of acquisition and its use in both the outpatient and inpatient settings.* CMS has assigned a Q code to the Kymriah product and a fee schedule equating to ASP+6%. This payment is specific to the outpatient Medicare setting, though it may be adopted as a benchmark by certain Medicaid programs for their pediatric patients in various care settings. The ASBMT established a Cell Therapy Coding & Reimbursement Task Force in early 2017, which is a group comprised of financial representatives from cell therapy programs administering CAR-T in various locations around the country. Task Force members were surveyed about the mark-up issue and reported that there is very limited ability to secure a mark-up on the product. Responses were between 0-4% mark-up above acquisition cost, depending on payer and center. A few programs were conducting detailed analyses of their costs in the preparation and handling of the product, including cell laboratory resources, specialized personnel and reporting requirements in the hopes of establishing a

Contact: Stephanie Farnia, ASBMT; StephanieFarnia@asbmt.org

mark-up that would account for costs outside of direct acquisition/purchase, but there has been limited success to this point.

On page 45, the authors note that a "bundled payment for CAR-T hospital admission is unknown at this time." As it pertains to Medicare admissions, there is not a specifically assigned Pre-MDC MS-DRG for CAR-T admissions. However, utilizing public information regarding CMS assignment of MS-DRGs based on principal diagnosis demonstrates that the most likely MS-DRG assignments will be MS-DRGs 840-842, with base payment amounts between $6,110-$16,736. Even if facilities utilize the maximum mark-up substantiated by public Medicare guidance for the product, no real dollar gains will be realized upon submission of these claims due to Medicare payment methodology. More detail on these issues are outlined in the ASBMT letter to CMS dated September 7, 2017, and additional letters to CMS/CMMI which can be found at www.asbmt.org/news-publications/advocacy. **Overall, the assumption of a $100,000 paid mark-up does not reflect actual practice and is not useful for purposes of this analysis.**

Finally, as ICER is employing a healthcare sector perspective for this analysis, we note that the use of mark-ups should actually be removed from the calculations entirely, as it is a transfer from one part of the healthcare sector (payer) to another (hospital). The case of integrated systems, such as Kaiser Permanente demonstrate the rationale for removing this from the analysis; the only markups that should matter are those from the manufacturer, as the manufacturer is outside of the healthcare sector.

3) The analysis of sequential treatment timelines or pathways is problematic based on the limited evidence available currently. The citation used to establish the expected time frame for receiving HCT after CAR-T was based on a limited number of pediatric patients with B-cell acute lymphoblastic leukemia (B-ALL) in a Phase I study. It does not include data on the adult diffuse large B-cell lymphoma (DLBCL) population. ICER should pursue another source of data for the time estimate and individualize by disease. The Center for International Blood and Marrow Transplant Research may have additional data available on this issue. In general, as numerous permutations of therapeutic pathways currently exist, and these will multiply further in the next few years, we need maturity of data before attempting to assess the financial impact and economic valuations of these therapies.

4) There are more recent analyses of the costs of HCT that may be useful. Additional sources are suggested below.
    a. Majhail NS, Mau LW, Denzen EM, Arneson TJ. Costs of autologous and allogeneic hematopoietic cell transplantation in the United States: a study using a large National Private Claims Database. Bone Marrow Transplant. 2013;48:294–300. [PMC free article] [PubMed]

Contact: Stephanie Farnia, ASBMT; StephanieFarnia@asbmt.org

b. Preussler JM, Denzen EM, Majhail NS. Costs and cost-effectiveness of hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2012;18:1620–1628. [PMC free article] [PubMed]
c. Khera N, Emmert A, Storer BE, et al. Costs of allogeneic hematopoietic cell transplantation using reduced intensity conditioning regimens. Oncologist. 2014;19:639–644. [PMC free article] [PubMed]

5) On page 13, the authors note that they are unable to locate any publicly available coverage policies regarding tisagenlecleucel. Health Net Community Solutions, which provides managed Medicaid benefits to certain counties in California, does have a publicly available clinical policy on this topic: Policy reference code CP.HNMC.XX, effective September 26, 2017.

6) On page 15, the authors note that non-Hodgkin lymphoma (NHL) is not specifically addressed in the CMS National Coverage Determination for Stem Cell Transplantation (110.8.1). This is correct – NHL is a "silent" indication and payment is determined by the MACs on a case-by-case basis. However, National Government Services (NGS), a MAC for regions J-06 and J-K, does provide a Local Coverage Article (A52879, Effective Date 10/01/2017) that includes coverage for allogeneic and autologous transplantation for the following types of lymphoma:

   a. Allogeneic:
      i. Primary refractory Hodgkin and non-Hodgkin lymphoma;
   b. Autologous:
      i. Anaplastic large cell lymphoma
      ii. Large cell lymphoma/B-cell lymphoma
      iii. Peripheral T-cell lymphoma
      iv. Primary central nervous system lymphoma

   This policy is not nationally representative, but may be a useful benchmark.

7) The ASBMT Value and Health Economics Steering Committee provided additional commentary on the methodology applied in the analysis:

   a. The modified societal perspective included caregiver costs, but did not include long-term productivity. Inclusion of this perspective is important in the B-ALL population.

   b. ICER should consider running a threshold analysis to find out what annual probability of relapse after 5 years would cause the cost effectiveness thresholds to be crossed.

Contact: Stephanie Farnia, ASBMT; StephanieFarnia@asbmt.org

c. ICER uses incremental comparison to no active treatment. If the report authors include no active treatment as an option, it should be compared to chemo, not CAR-T. A legitimate analysis should not skip the next-least-effective non-dominated treatment.

The ASBMT welcomes the opportunity to provide input to the ICER process for evaluating CAR-T therapy. ASBMT peer-elected leaders, member clinicians and policy staff are available as a resource for issues associated with HCT, CAR-T and other cellular therapies. Please do not hesitate to reach out whenever we may be of assistance.

Krishna Komanduri, MD
ASBMT President, 2017-2018
Health Policy Staff Contact: Stephanie Farnia, Director, Health Policy;
StephanieFarnia@asbmt.org; (847) 725-2316