AMERICAN SOCIETY of GENE & CELL THERAPY

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Dear Ms. Syrek Jensen, Dr. Szarama and Dr. Paserchia:

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to provide comments to the Centers for Medicare & Medicaid Services (CMS) regarding the proposed decision memo on the national coverage analysis for chimeric antigen receptor T-cell (CAR T-cell) therapy. ASGCT is a nonprofit professional membership organization comprised of more than 3,000 scientists, physicians, and other professionals working in gene and cell therapy in settings such as universities, hospitals, and biotechnology companies. The mission of ASGCT is to advance knowledge, awareness, and education leading to the discovery and clinical application of genetic and cellular therapies to alleviate human disease.

Maximizing patient access to approved gene and cell therapies is integral to this mission. The Society appreciates CMS efforts to make these lifesaving therapies available to patients, and shares the goal of advancing scientific knowledge about the benefits and risks of CAR T-cell therapies. ASGCT maintains, however, that current Medicare coverage of CAR T-cell therapies is appropriate, as stated in comments to the Agency dated June 15, 2018.

The Society is concerned that, as currently drafted, the proposed decision memo including coverage with evidence development (CED) may limit patient access to CAR T-cell therapies for Food and Drug Administration (FDA)-approved indications now and in the future. The additional administrative burden imposed on providers by coverage with evidence development (CED) may result in providers opting out of CED participation, thereby not providing the therapy to Medicare beneficiaries. ASGCT respectfully requests that the Agency consider the specific concerns and related recommendations below in order to ensure medically appropriate access to these therapies.

Patient Eligibility Requirements

The proposed decision memo requires that a patient has relapsed or refractory cancer for CMS to cover CAR T-cell therapy. While the two FDA-approved CAR T-cell products are only approved for relapsed or refractory indications,[i,ii] future FDA-approved indications and products have the potential to be first-line indications.[iii] To ensure patients do not experience limitations in accessing, or lapses in coverage for, FDA-approved CAR T-cell products with first-line indications, ASGCT recommends removing "relapsed or refractory," and substituting the following or similar wording as the first eligibility requirement:

> *A1. Patient has:*
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> *a. a cancer for which treatment with an FDA-approved CAR-T targeted therapy is indicated OR a cancer for which treatment with an FDA-approved CAR-T targeted therapy is identified in the National Comprehensive Cancer Network Drugs & Biologics Compendium (category 1 or 2).*

Providing sufficient scope of coverage in the final decision memo to address upcoming applications of CAR T-cell therapy is of utmost importance in providing timely patient access to potentially lifesaving treatments, as more of the numerous therapies in the research pipeline receive FDA approval.

Site of Care

ASGCT supports strong criteria for qualified medical facilities that provide these therapies to ensure the best possible patient outcomes. We agree that facilities should meet the FDA's Risk Evaluation and Mitigation Strategies criteria, as well as the criteria proposed in the decision memo—that the facility has a cell therapy program consisting of an integrated medical team with consistent protocols, procedures, quality management, and clinical outcomes; a designated care area that protects the patient from infectious agents; and written guidelines for patient communication, monitoring, and transfer to an intensive care unit. However, the Society is concerned that by referring to these facilities as "hospitals," CMS may be limiting the number of sites available to patients that may otherwise be qualified except for how they are licensed or paid. We recommend changing the term "hospital" to "medical facility" throughout the proposed decision memo to prevent potential unnecessary restrictions in coverage due to a lack of clarity in the terminology, and focus only on the standards that these facilities must meet.

Treatment Criteria

ASGCT is pleased that the proposed treatment criteria cover FDA-approved biologicals that meet one of the following two criteria—either providing targeted therapy for a known antigen expressed in the patient's cancer according to an FDA indication; or indicated for use identified in the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium. However, the proposed memo specifies that CMS would specifically cover autologous treatment with T cells expressing at least one CAR. While current FDA-approved therapies utilize autologous CAR T-cells, clinical trials are imminent utilizing allogeneic CAR T cells.[iv] This innovation has the potential to change these therapies from patient-specific products to patient population-specific products, sometimes referred to as "off-the-shelf" CAR T-cell therapies. ASGCT therefore recommends removing the word "autologous" as a treatment criterion in the following sentence, to accommodate potential FDA approvals of allogeneic CAR T-cell therapy products:

> "The Centers for Medicare and Medicaid Services (CMS) proposes to cover treatment with T cells expressing at least one chimeric antigen receptor (CAR) through coverage with evidence development when prescribed by the treating oncologist …"

Patient-Reported Outcomes

ASGCT members support efforts to make drug development and the delivery of health care more patient-centered, and believe that the use of patient-reported outcomes (PROs) can help bolster these efforts. From a scientific

perspective, the society is concerned by the NCA's proposed inconsistent collection of PROs only for CAR T-cell therapies, as well as use of two different tools.

A consideration in determining whether to collect this data following CAR T-cell therapy is whether the data is also being collected for an appropriate comparison group, such as historical controls of a cohort of patients receiving alternative therapeutic regimens. Furthermore, if CMS does require collection of PROs, the Society recommends using only a single metric for improved compilation of data, with the most appropriate questions for long-term follow up of patients. The Patient-Reported Outcomes Measurement Information System (PROMIS) is a well validated instrument that meets this requirement. The alternative metric listed is the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events. Collection of information on adverse events would not be applicable beyond the first of four follow-up points occurring between three and 24 months after the procedure.

Registry Considerations

ASGCT encourages the Agency to align the effective date for data collection requirements with the date of broad availability of at least one patient registry with capability to collect required data sets in order to avoid lapses in coverage, which could have fatal consequences for patients with no other treatment options. To facilitate timely initiation of data collection, we recommend that CMS list the Center for International Blood and Marrow Transplant Research (CIBMTR) registry in the final decision memo as an approved patient registry, as it is already being utilized to collect patient data for FDA-required post-marketing studies. FDA post-market study data requirements are consistent with the CMS proposed data requirements except for PRO data. If the patient registry is prepared to collect all required information except for the PRO data at the established effective date of data collection, ASGCT requests that CMS does not delay coverage, but rather allows PRO data to be incorporated as soon as possible. Additionally, the Society recommends CMS clarify that the therapy will be covered for patients who have already undergone lymphocyte harvesting at the time the final memo is issued. These patients will not have reported data elements before beginning therapy, but need to be assured their time-sensitive therapy will be completed and covered.

The Society also requests CMS indicate that the patient registry may collect PRO data at later time points after providers obtain initial patient consent to ease the long-term administrative burdens on providers. ASGCT further requests Agency clarification regarding how CMS will consider coverage for patients who do not consent to participation in PRO data collection.

Thank you for your consideration of these comments. Please consider ASGCT a resource as you work to finalize the decision memo.

Sincerely,

Michele P. Calos, PhD
ASGCT President

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[i] Kite Pharma, Inc. (2017). *Yescarta: Prescribing information.* Santa Monica, CA.
[ii] Novartis. (2017). *Kymriah: Prescribing information.* East Hanover, NJ
[iii] Efficacy and safety of axicabtagene ciloleucel as first-line therapy in participants with high-risk large B-cell lymphoma (ZUMA-12). (2018). Retrieved from https://clinicaltrials.gov/ct2/show/NCT03761056. (Identification No. NCT 03761056).
[iv] Dose-escalation study of safety of PBCAR0191 in patients with r/r NHL and r/r B-cell ALL. (2018). Retrieved from https://www.clinicaltrials.gov/ct2/show/NCT03666000?term=precision+biosciences+allogeneic+CAR+T&rank=1. (Identification No. NCT03666000).