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RE: National Coverage Analysis (NCA) Tracking Sheet for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N)

Dear Ms. Syrek Jensen and Drs. Szarama and Paserchia:

The Society for Immunotherapy of Cancer (SITC) appreciates the opportunity to respond to the Centers for Medicare & Medicaid Services' (CMS') decision to open a National Coverage Analysis (NCA) for Chimeric Antigen Receptor T-Cell (CAR-T) therapies. With nearly 2,000 members representing 17 medical specialties, SITC is the world's leading member-driven organization specifically dedicated to improving cancer patient outcomes by advancing the science and application of cancer immunotherapy. SITC aims to make cancer immunotherapy a standard of care.

The Food & Drug Administration (FDA) approvals of Kymriah® (tisangenlecleucel) and Yescarta® (axicabtagene ciloleucel) as medically accepted anti-cancer treatments when the use is on-label and presumed medically accepted treatments when supported by compendia, were significant milestones in ensuring patient access to these novel immunotherapies.

SITC wants to assure the process of conducting an NCA and any subsequent policy implemented at the conclusion of NCA process does not irreparably hinder access to these FDA-approved lifesaving treatments or measurably slow the development of innovative, new CAR-T therapies. ***We, therefore, urge CMS to consider the following key points as it goes through the NCA process relative to the unique aspects of CAR-T therapy.***

I. The use of CAR-T therapies involves a onetime administration of the treatment with any adverse events representing at the time of administration.

As a personalized medicine, the administration of CAR-T therapies, and immunotherapies more broadly, requires intimate and tailored patient-physician interaction and decision-making. Historically, CMS has

been understandably resistant to interfering with the ability of physicians and patients to manage their care decisions when considering on-label medical solutions, like CAR-T therapies.[1]

In the case of the approved CAR-T therapies, the FDA has already outlined a Risk Evaluation and Mitigation Strategy (REMS), including (a) requiring certification of sites administering the CAR-T therapies, (b) ensuring access to tocilizumab, and (c) mandating training for staff involved in the prescribing, dispensing, or administering of the treatment.[2] With these safeguards in place, the need for evaluation by an NCD is unnecessary and duplicative of the FDA's efforts.

Moreover, data thus far indicate that most adverse event will within one week of infusion, making the management and response both predictable and reversible compared to other therapies.

UnitedHealthcare's (UHC's) concern regarding the financial stability of these therapies within the Medicare Advantage (MA) program should be addressed outside of the NCA process. The NCA process is designed to address a need to enable access to a specific class of patients, not to address the cost of care.

II. Data to date on FDA approved indications demonstrate CAR-T cures a significant percentage of patients with diseases that are otherwise rapidly fatal and for which there are no other good therapeutic options.

The long-term curative potential of CAR-T therapies has been shown in studies reported as recent as June 2018[3]. Currently, the FDA approved use of CAR-T therapies is limited to a therapy of last resort; however, with one administration of the therapy these patients, who otherwise would succumb to their disease, are cured of cancer.

III. Rapid decisions for each individual patient on whether to proceed with therapy are required as a delay of even a few days could have a major impact on the likelihood of success.

Patients eligible for the approved CAR-T therapies are particularly vulnerable as CAR-T is the final treatment available to them and their life expectancy is very limited. Any delay in administration of the CAR-T may result in death or negatively impact patient outcomes for this patient population.

In addition, patients and hospitals are already required to complete significant consent and reporting processes to comply with the Center for International Blood and Marrow Transplant Research (CIBMTR) and post-market studies.

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[1] Social Security Act, Section 1801.

[2] What is the Yescarta REMS Program? https://www.yescartarems.com/; Risk Evaluation and Mitigation Strategy (REMS), http://www.kymriah-rems.com/.

[3] Locke FL, Ghobadi A, Jacobson CA, Jacobsen ED, Miklos DB, Lekakis LJ, Braunschweig I, Oluwole OO, Lin Y, Siddiqi T *et al*: Durability of response in ZUMA-1, the pivotal phase 2 study of axicabtagene ciloleucel (Axi-Cel) in patients (Pts) with refractory large B-cell lymphoma. *Journal of Clinical Oncology* 2018, 36(15_suppl):3003-3003.

We ask CMS to consider that should the NCA result in a coverage with evidence development (CED) decision, hospitals would have an additional layer of reporting and administrative burden that could influence a centers willingness to administer CAR-T therapies.

Patients would also be required to complete an additional consent form and subject themselves to the study agreement if they want to receive these life-saving treatments, putting them in an untenable and unethical position.

IV. Any NCD would hinder future innovation of novel CAR-T therapies.

As a disruptive and groundbreaking anti-cancer treatment, CAR-T therapies have the potential to revolutionize cancer care and treatment. With over 1,500 immunotherapy clinical trials currently active, an NCD developed today would not have the scope to address coverage of new CAR-T therapies or novel applications of currently approved therapies. Any NCD would disincentivize investment in and development of the therapies currently in the pipeline.

As a professional organization, SITC actively supports on-going efforts to better study and define the value of CAR-T therapy, including a deeper understanding of the economic impact on patients, payors, industry and other stakeholders.

We also welcome the opportunity to work with CMS to identify important areas for research and consensus building and remain eager to serve as a professional resource to CMS during this time of rapidly developing advances in the field.

We again appreciate the opportunity to submit our comments and concerns regarding the NCA on CAR-T therapies. We urge CMS to consider the above key points as it goes through the NCA process relative to the unique aspects of CAR-T therapy and ask that you keep patient access, innovation, and the practice of medicine as priorities throughout your process.

We respectfully offer our society's leadership and expertise in future considerations impacting the field of cancer immunotherapy.

Should you have any questions, please do not hesitate to contact STIC Executive Director, Tara Withington, at twithington@sitcancer.org.

Sincerely,

Lisa H. Butterfield, PhD
SITC President