Alliance for Regenerative Medicine

October 13, 2020

Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

Re: Comments to Draft Scoping Document on Anti B-Cell Maturation Antigen CAR T-cell and Antibody Conjugate Therapy for Triple Class Refractory Multiple Myeloma

## Introduction

The Alliance for Regenerative Medicine (ARM) is pleased to provide our comments in response to the Institute for Clinical and Economic Review (ICER) September 22, 2020 draft Background and Scope Document on Anti B-Cell Maturation Antigen CAR T-cell and Antibody Conjugate Therapy for Triple Class Refractory Multiple Myeloma ("Scoping Document")[1]. ARM is the leading international advocacy organization dedicated to realizing the promise of regenerative medicines and advanced therapies. ARM promotes legislative, regulatory and reimbursement initiatives to advance this innovative and transformative sector, which includes cell therapies, gene therapies and tissue-based therapies. In its 11-year history, ARM has become the voice of the sector, representing the interests of 360+ members worldwide, including small and large companies, academic research institutions, major medical centers and patient groups. Although focused on one type of cancer, the Scoping Document raises critical issues for ARM members because of its potential negative impact on the development of the therapies under review and future therapies. ARM is concerned that the timing of the review will not take into account FDA's perspective on the appropriate patient population (i.e., through the label) and that of expert providers' perspectives (i.e., through recognized compendia) and will therefore unjustifiably raise questions and doubt in the technology that could ultimately harm market access.

With the emergence of these therapies, our society is entering an unprecedented era of potentially curative treatments for patients. ICER has previously acknowledged, "the science is undeniably exciting" and can "reflect extreme magnitudes of lifetime health gains and cost offsets that are far beyond those generated by traditional therapies." More recently, ICER has stated, "Cell and gene therapies are starting to provide truly transformative advances for patients and their families, particularly those with conditions for which there has not been any effective treatment before." In light of these comments, ARM questions why ICER is choosing to conduct this review on therapies that have not yet even been approved by FDA. ARM believes that this assessment is premature and inappropriate, especially to include antibody drug conjugate therapy in the review because it is simply not comparable.

## Stakeholder Input

ARM believes that independent scientific evaluations of clinical and economic evidence supporting the utilization of FDA therapies is critical. However, such analyses should focus on the unique benefits of a new technology before considering issues of short-term costs and/or the need for innovative payment models. Such an approach optimizes patient access to the most appropriate therapy to treat their disease. Further, ARM believes that this initial input did not include a broad enough range of stakeholders. Increasing transparency and ensuring all stakeholders have input will allow everyone to gain a much better understanding of the true value of this emerging

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[1] https://icer-review.org/wp-content/uploads/2020/08/ICER_Multiple-Myeloma_Draft-Scope_092220.pdf

technology.[2] We appreciate ICER's interest in engaging with the stated experts, but we also note that broader engagement is necessary to obtain input from expert bodies, especially in the nascent field of HTA for potentially curative therapies. ARM has had interactions with experts from methodological bodies such as the International Society of Pharmacoeconomics and Outcomes Research (ISPOR), Health Technology Assessment International (HTAi) and the Second Panel on the Cost-Effectiveness in Health and Medicine[3]. These organizations have published extensively on key methodological issues in evaluating new therapies. ARM hopes that ICER will continue to seek participation from these experts when evaluating new issues.

**Report Aim**

ICER states that this project will evaluate the health and economic outcomes of the therapies and will include both quantitative and qualitative comparisons across treatments to ensure that the full range of benefits and risk are considered. ARM appreciates this intention but has concerns about such comparisons being made across therapies that treat different patient populations. A close review of the clinical trials for the therapies included in the assessment would reveal that patients treated with cell therapies were quite different from patients treated by non-cell therapies. There exists an "inherent selection bias" when physicians decide to treat with cell or non-cell therapies, which is not fully captured in patient characteristics and eligibility criteria of clinical trials and would extend to real world setting too. Further, in the case of cell therapies, patients generally have already progressed on non-cell therapies (and likely, many times) and have run out of options, which the cell therapy now provides. It would be irrelevant to use the non-cell therapy population as a comparator in that situation. This important difference should be considered in light of ICER's intentions with this review, as any comparison across these therapies would not prove useful because clinical practice patterns consider different patient types. Furthermore, the economic model as detailed in the Scoping Document does not reflect standard clinical decision-making to the disease state of interest. Should ICER proceed with this assessment ARM is concerned that it would set precedence for ICER to draw inappropriate comparisons across therapies and yield an assessment that has no relevance to clinical practice. With a flawed approach applied to therapies that treat different patient populations, the report will not be well positioned to achieve ICER's stated aim.

**Scope and Methodology of the Comparative Value Analyses**

All clinical interventions should be first appraised based on their clinical merit for patients and benefits to families and caregivers, with deference to FDA's expertise and judgement. Discussions around society's willingness and ability to pay should take place subsequently and should be considered/determined by those who are directly impacted by a potential treatment choice based on the individual clinical circumstances at issue, not made in the abstract by third-party observers such as ICER. Collectively, we should make every effort to ensure patients have access to innovative new therapies in a timely manner, especially in the case of severe or life-threatening conditions, and that incentives for innovation remain in place, so that the pace of innovation is not hindered by undue challenges in market access and commercialization for this new class of transformative therapies.

In prior public statements, ARM has been clear that HTA frameworks are not flexible enough to accommodate potential cures and have not yet progressed to consistently capture the full product value due to issues including: the short term time frame for assessing affordability versus the long-term timeframe for assessing value; variability in ability and willingness to pay (and applicability of ICER threshold) based on degree of unmet medical need addressed; and the subjectivity of incorporating contextual considerations such as caregiver and societal impacts into a quantitative framework[4].

[2] https://icer-review.org/wp-content/uploads/2020/08/ICER_MM_Key_Stakeholders_092720.pdf

[3] Peter J. Neumann et al, *Cost-Effectiveness in Health and Medicine* (Oxford Scholarship Online, November 2016).

[4] See March 29, 2017 ARM letter to ICER regarding the proposed update to the ICER Value Assessment Framework.

ARM believes that ICER has a responsibility to conduct balanced evidence assessment as well as updates in economic evaluation methods that reflect the unique and broad benefits of these therapies. Reserving the public dissemination of proposed value-based payment benchmarks until a more comprehensive data set (including real world evidence) is adequate to support the validity of the underlying assessments, as well as rigorously updating assessments as evidence that reflects clinical outcomes, patient and caregiver benefits and societal impacts becomes available should be more formally reflected in ICER methods and processes.

Prematurely determining the 'fairness' of the price of highly innovative therapies for which evidence on the duration and full spectrum of benefits is not yet known does not serve patients, their families, caregivers or society, especially if it results in undue barriers to patients receiving potentially life changing treatments. ARM believes it is important to separate methodological issues from affordability and policy considerations. ICER could also play an important role in supporting industry and payer efforts to design new payment models and systems that accommodate uncertainty in long-term outcomes for newly approved innovative therapies while also rewarding unprecedented long-term performance and innovation.

ARM believes that the uniform application of cost/effectiveness thresholds in value assessments across all product and disease types is not appropriate. ICER's current approach relies largely on QALY-based cost-effectiveness models. ARM believes that the continued use of the QALY measure in ICER sensitivity analysis informing ICER's analysis is likely inappropriate given the unique nature of these therapies. ARM does not believe that the QALY is an appropriate measure of value. We furthermore believe that the evidence value of life-years gained (evLYG) approach is also a flawed way to compare different treatments within the same disease area. The evLYG does not account for differences in quality of life that may differ between treatments due to their administration routes, mechanisms of action, or other factors. This is particularly inappropriate when comparing chronically administered therapies compared to single-administration therapies. The side effects of chronic use may continuously impact patients' quality of life beyond disease-related factors. In contrast, single-administration treatments may only transiently impact quality of life while providing similar or better benefits on survival and other disease metrics over the long-term.

Rather, ARM suggests that ICER should use multi-criterion decision analysis (MCDA) to address this limitation.[5] Developed from the field of systems engineering, MCDA measures how different treatments perform across a variety of attributes and explicitly asks the decision maker to weigh these different attributes. MCDA can be used to quantify these contextual considerations and decision makers can use MCDA to examine how different prioritization affects treatment recommendations. MCDA may be useful when some key attributes of MCDA-informed value include cost or benefits received by society, but that are not captured by individual decision making or within ICER's CEA model. ARM encourages ICER to continue to collaborate with the health economic field to monitor the potential future inclusion of these dimensions. ARM appreciates the opportunity to provide our perspective on these important issues. Please do not hesitate to contact me if you have any questions.

Sincerely,

Robert J. Falb,
Director, U.S. Policy and Advocacy

[5] Phelps CE, Madhavan G. Valuing Health: Evolution, Revolution, Resistance, and Reform. Value in Health. 2019 May 1;22(5):505-10