Alliance for Regenerative Medicine

March 8, 2021

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

Re: Comments to Draft Evidence Report on Anti B-Cell Maturation Antigen CAR T-cell and Antibody Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma

Introduction

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to submit the following comments to the Institute for Clinical and Economic Review (ICER) February 11, 2021 draft report on Anti B-Cell Maturation Antigen CAR T-cell and Antibody Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma ("Draft Evidence Report").[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 global voice of the sector, representing the interests of 380+ members worldwide, including small and large companies, academic research institutions, major medical centers and patient groups.

Although focused on one type of rare cancer, the Draft Evidence Report raises important 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 prevents ICER from taking into account the FDA's perspective on the appropriate patient population (i.e., through the label), that of expert providers' perspectives (i.e., through recognized compendia), and the technology's durability. Consequently, ARM is concerned that the Draft Evidence Report may harm market and patient access.

With the emergence of these therapies, our society is entering an unprecedented era of potentially curative treatments for patients. ICER seems to agree by previously stating that , "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. Additionally, ICER 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

[1] Lee SJ, McQueen RB, Beinfeld M, Fluetsch N, Whittington MD, Pearson SD, Ollendorf DA. Anti B-Cell Maturation Antigen CAR T-cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma; Draft Evidence Report. Institute for Clinical and Economic Review, February 11, 2021. https://icer.org/assessment/multiple-myeloma-2021/#timeline

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treatment before." ARM shares ICER's excitement regarding the science but is concerned ICER's review is ahead of FDA approval and post market data will lead to incomplete assessments and conclusions regarding the magnitude and cost offsets that these therapies can bring to patients and the overall healthcare system.

Draft Evidence Report Initial Conclusions

ARM appreciates the Draft Evidence Report findings that the evidence suggests that the chimeric antigen receptor T-cell therapies examined improve outcomes for triple-class refractory MM patients, with higher rates of response and longer survival than treatment with current therapies.

Consistent with traditional evidence reviews, ICER raises some uncertainties and limitations to its conclusions based on clinical trial design and the selection of an appropriate comparator. ARM's initial comments[2] raised some of these concerns and predicted these short fallings. Specifically, ARM stated that comparisons being made across therapies that treat different patient populations and that 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. ARM notes that while ICER did not make these direct comparisons, the many Tables in the Draft Evidence Report could easily lead and confuse the reader towards making these inappropriate conclusions.

Further, ARM requests that ICER detail the process physicians followed in making the decision to refer to a clinical trial. This information will further clarify the patient characteristics and eligibility criteria of the patients who entered the clinical trials and therefore may guide future physician decision when treating in the real world setting. Further, in the case of cell therapies, patients generally have already failed on non-cell therapies (and likely, many times) and have run out of options, which the cell therapy now provides, which is not well documented n this report. ARM remains concerned that this Draft Evidence Review sets an inappropriate precedence for ICER to draw non-evidence based comparisons across therapies that yields an assessment that is not instructional on clinical practice.

Stakeholder Input

As stated in our initial comments to this Draft Evidence Report, ARM believes that independent scientific evaluations of clinical and economic evidence supporting the utilization of FDA approved therapies is critical, however at the appropriate time. These analyses should focus on the unique benefits of a new technology over the period of time in which its treatment effect is observed in a real-world setting post-approval before considering issues of short-term costs and/or even the need for innovative payment models, which may not be appropriate given this patient population and the longer-term efficacy readouts. Such an approach optimizes patient access to the most appropriate and innovative therapy to treat their disease.

ARM reiterates that this initial input did not include a broad enough range of stakeholders to lead to a true assessment and understanding of the value of this technology. ICER should focus on increased transparency and broader input that will likely lead to a much better appreciation of the

[2] See October 13, 2020 ARM letter to ICER "Comments to Draft Scoping Document on Anti B-Cell Maturation Antigen CAR T-cell and Antibody Conjugate Therapy for Triple Class Refractory Multiple Myeloma."

true value of this emerging technology.[3] 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.[4] These organizations have published extensively on key methodological issues in evaluating new therapies. ARM recommends that ICER will seek participation from these experts when drafting its final report and in the future when evaluating new issues.

Scope and Methodology of the Comparative Value Analyses

In prior public statements, ARM has been clear that current 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.[5]

ARM recommends that ICER incorporate updates in economic evaluation methods that reflect the unique and broad benefits of these therapies. In this regard, ARM recommends that this process leads ICER to conduct these types of review post-FDA approval and recommends the use of updated analytical tools for these emerging healthcare technologies. Specifically, when ICER conducts its review it also should include a multi-criterion decision analysis (MCDA) tool as part of its assessment.[6] 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. Finally, MCDA could also capture varying priorities based on stakeholder; for example, collect patient priorities versus other stakeholders, and therefore incorporate patient input more extensively than they do currently.

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.

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

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

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

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

Sincerely,

Robert J. Falb
Director, U.S. Regulatory Affairs