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Commentary

If They RECUR, You Should Refer: A Community Oncologist Patient ID Roundtable Summary

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Chimeric antigen receptor-modified T cell (CAR-T) therapy has become a critical part of the armamentarium for the treatment of relapsed/refractory hematologic malignancies. As our experience with CAR-T therapy grows and new data emerge, the identification of suitable patients has become more complex. The Community Oncologist Patient ID Roundtable, held on May 16, 2023, brought together 3 professional societies— (American Society for Transplantation and Cellular Therapy [ASTCT], Association of Community Cancer Centers [ACCC], and Association of American Cancer Institutes [AACI])—with the aim of developing a standardized framework to enable community oncology care teams to assess patients more easily for CAR T consultation, with a focus on large B cell lymphoma (LBCL). The main objectives of this discussion were to achieve consensus on a framework for rapid patient identification for a CAR-T consult in LBCL and discuss potential channels, partners, and next steps for dissemination of information and community education.

When considering a patient for referral to a CAR-T therapy specialist, important factors include the disease indication, clinical fitness (including cardiac, pulmonary, renal, hepatic, neurologic, immune dysfunction, or other significant comorbidities; clinical deterioration; and performance status), and nonclinical factors, such as the time required for treatment/recovery, distance from an authorized treatment center, out-of-pocket costs and other financial barriers, caregiver status, and employment status [1–3]. Rapid identification and consultation, ideally at the earliest indications of first-line treatment failure, can increase the likelihood that patients will receive CAR-T therapy expeditiously and benefit maximally from treatment [4–7]. Many oncologists may find it difficult to ascertain the appropriateness or optimal timing of referral, however.

An effective framework for CAR-T patient identification should reflect the clinical and nonclinical patient factors that influence suitability for CAR-T therapy consultation. It should provide clear guidance that is not overly restrictive and

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includes timing and actions for rapid decision making. Such a framework should be adaptable as clinical guidelines and the treatment landscape evolve over time, serve as a readily applicable educational resource for community oncology care teams and patients, and withstand pressure testing by multiple stakeholders in the CAR-T therapy community.

Early patient identification increases the chance of referring eligible patients with LBCL to CAR-T specialists in time to optimize treatment response and improve outcomes. One key discussion at the roundtable centered around challenges faced by community oncologists in identifying patients appropriate for CAR-T consultation. These included a lack of central guidance, insufficient awareness of patient resources, minimal real-world CAR-T experience including feedback on CAR-T outcomes, and limited exposure to patients with LBCL. In this context, a streamlined framework would empower community oncologists to refer potential patients more confidently for consideration of CAR-T therapy and strengthen their pivotal role in expanding access to this potentially curative therapy.

A factor prioritization exercise identified 5 key factors to optimize CAR-T consultation and access: (1) relapsed/refractory disease, which is the minimum criterion and consensus trigger for referral; (2) availability of support for patients, including financial support, across the continuum of care; (3) communication across multiple levels, including bidirectional communication between CAR-T therapy centers and community oncologists; (4) an understanding that comorbidities would be evaluated on a case-by-case basis by cellular therapy specialists and are not necessarily a contraindication to CAR-T therapy; and similarly, (5) an understanding that advanced age in general should not be a barrier to consultation.

Participants universally agreed that the presence of LBCL that is relapsed after or refractory to first-line standard-of-care treatment is the most critical consideration. Dr Peter Riedell of the AACI deemed relapsed/refractory disease "the most important consideration when considering a CAR T consult." Similarly, Dr David Porter of the ASTCT cited "anyone with relapsed or refractory disease" as the "key determinant" for consult eligibility.

Roundtable participants next discussed the role of psychosocial and financial challenges for patients under consideration for CAR-T therapy and stressed the importance of caregivers and support for essential needs. Dr Riedell reminded the group, "It is not just the drug cost. It is the parking, other costs to support treatment and around treatment [such as] caregiver accommodation. . .So [cumulative cost] is certainly a significant factor." Although cost is admittedly a major obstacle, it was emphasized that it should not prevent any patient from being considered for consultation with a cell therapy specialist. As stated by Judy Ebmeier of the ACCC, "It is important to connect the patient with services for psychosocial support, transport. . .[I]t is key for these patients."

Comorbidities and age also were cited as important factors in overall decision making around CAR-T therapy but, importantly, not contraindications to cellular therapy consultation. As Dr Porter stated, "Age, no [it should not be a barrier]. . .I personally don't think age should be highlighted as a limiting factor. Leave that up to the treatment center." In real-world experience, axicabtagene ciloleucel, for instance, demonstrated a 57% improvement in overall response rate over standard chemoimmunotherapy in patients age $\geq$65 years versus a 46% improvement among those age $<$65 years, underscoring the potential benefit for older patients [8]. Similarly, the presence of comorbidities is an important consideration for specialists when evaluating and counseling patients around CAR-T therapy but should not preclude referral; even patients with severe comorbidities, such as end-stage renal disease on dialysis, are being successfully treated with CAR-T therapy [9]. Multidisciplinary collaborations with case workers, social workers, advocacy foundations (eg, Leukemia & Lymphoma Society, Lymphoma Research Foundation), and patients' financial counselors should be explored to potentially mitigate financial toxicity and issues surrounding transportation and psychosocial distress.

In a survey among participants, the slogan "If they RECUR, you should refer" was deemed most effective, with RECUR representing Relapsed/refractory LBCL, Every age and comorbidity, Caregiver support, Urgency to recommend consult, and Receive patients returning post-CAR-T therapy. "If they RECUR, you should refer" encapsulates the roundtable's conclusions and provides a framework for oncologists to identify patients suitable for CAR T cell consultation and in turn allows them to facilitate access to potentially curative therapy for relapsed/refractory LBCL.

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REFERENCES

1. Auletta JJ, Khera N, DeMartino P, et al. Assessing Medicaid coverage for hematopoietic cell transplantation and chimeric antigen receptor T cell therapy. A project from the American Society for Transplantation and Cellular Therapy and the National Marrow Donor Program ACCESS Initiative. *Transplant Cell Ther*. 2023;29:713–720.
2. Auletta JJ, Holter-Chakrabarty J, Jain T, et al. Proceedings of the 2023 Second Annual ASTCT-NMDP ACCESS Initiative Workshop. Transplant Cell Ther. September 29, 2023 [Epub ahead of print]. https://doi.org/10.1016/j.jtct.2023.09.026.
3. Mikhael J, Fowler J, Shah N. Chimeric antigen receptor T-cell therapies: barriers and solutions to access. *JCO Oncol Pract*. 2022;18:800–807.
4. Jain T, Bar M, Kansagra AJ, et al. Use of chimeric antigen receptor T cell therapy in clinical practice for relapsed/refractory aggressive B cell non-Hodgkin lymphoma: an expert panel opinion from the American Society for Transplantation and Cellular Therapy. *Biol Blood Marrow Transplant*. 2019;25:2305–2321.
5. O'Rourke K. ASCO releases guideline on CAR T-cell therapy: a multidisciplinary team's recommendations help in the recognition, workup, evaluation, and management of the most common chimeric antigen receptor (CAR) T-cell-related toxicities. *Cancer*. 2022;128:429–430.
6. Kanate AS, Majhail N, DeFilipp Z, et al. Updated indications for immune effector cell therapy: 2023 guidelines from the American Society for Transplantation and Cellular Therapy. *Transplant Cell Ther*. 2023;29:594–597.
7. Perales MA, Anderson Jr LD, Jain T, et al. Role of CD19 chimeric antigen receptor T cells in second-line large B cell lymphoma: lessons from phase 3 trials. An expert panel opinion from the American Society for Transplantation and Cellular Therapy. *Transplant Cell Ther*. 2022;28:546–559.
8. Lunning M, Wang H-L, Hu Z-H, et al. Outcomes of axicabtagene ciloleucel in comparison with chemoimmunotherapy (CIT) in an elderly population for treatment of relapsed or refractory (r/r) large B-cell lymphoma (LBCL) after two or more lines of prior therapy. *Blood*. 2022;140:1852–1855.
9. Hunter BD, Hoda D, Nguyen A, et al. Successful administration of chimeric antigen receptor (CAR) T-cell therapy in patients requiring hemodialysis. *Exp Hematol Oncol*. 2022;11:10.