Optimization of CAR-T therapy utilization in multiple myeloma

Introduction to CAR-T therapy in multiple myeloma (MM)

During CAR-T therapy, a patient's own T cells are engineered to express a CAR that targets BCMA, which is expressed on normal and malignant plasma cells but not on hematopoietic stem cells. This enables the T cells to find and destroy MM cells after manufacturing, the CAR-T cells are infused into the patient's body to attack tumor cells and initiate an immune response that promotes further anticancer activity[1]

Administration of CAR-T therapy is a resource-intensive process that requires careful coordination between referring physician and multidisciplinary teams

Considerations prior to CAR-T therapy

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Two CAR-T products are currently approved for the treatment of adult patients with RRMM: cilta-cel in patients refractory to lenalidomide after ≥1 prior LOT,* and ide-cel in patients after ≥2 prior LOT†[1,2,3]

Treatment stage	Key considerations
Patient eligibility, referral and selection	• Early referral of patients can help facilitate discussions about therapy considerations to optimize leukapheresis[4] • The patient must be clinically stable for the CAR-T manufacturing and therapy processes[1] • Prior exposure to BCMA-targeted therapy can negatively affect clinical response to CAR-T cells[4]
Leukapheresis	• The referring physician and CAR-T therapy physician should discuss choice/timing of holding therapy before leukapheresis[4] • Key considerations to optimize the collected T cells for manufacturing include drug half-life, drug effect on number/fitness of T cells, and clinically feasible washout period[4] • Multiple factors can impact T-cell fitness and clinical efficacy[4] • Duration of washout periods should be considered; adherence to recommended washout times is considered crucial for optimizing manufacturing success[1]
Bridging therapy	• Choice of BT should be a collaborative effort between the referring physician and CAR-T therapy physician, and individualized based on various patient-specific factors[1] • Enhanced BT‡ has been recommended to reduce baseline tumor burden to minimize the risk of neurologic AEs after BCMA CAR-T therapy[1] • If BT is used, consider completing at least 1 cycle prior to lymphodepletion and CAR-T infusion and a washout period of at least 1 week (washout period of up to 2 weeks have been used in clinical trials)[1]
Infection screening	• CAR-T therapy should not be administered in patients who might have active infections[4] • Additional screenings might be appropriate depending on the patient-specific factors[4]
Lymphodepletion	• Check the patients' renal function and renally dose adjust LDCs (cyclophosphamide and fludarabine) drugs to reduce the risk of toxicity[1]

*Including a PI and an immunomodulatory drug. †Including a PI, immunomodulatory drug and an anti-CD38 mAb.
‡Enhanced BT allows fewer restrictions on type and duration of BT.
AE, adverse event; BCMA, B-cell maturation antigen; BT, bridging therapy; CAR-T, chimeric antigen receptor T cell; CD, cluster of differentiation; LDC, lymphodepleting chemotherapy; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma.

1. Ailawadhi S, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24(5)e:217–225.
2. CARVYKTI® (ciltacabtagene autoleucel). Prescribing Information. Horsham, PA: Janssen Biotech, Inc.
3. ABECMA® (idecabtagene vicleucel). Prescribing Information. Cambridge, MA: Celgene Corporation, a Bristol-Myers Squibb Company.
4. Lin Y, et al. *Lancet Oncol.* 2024;25:e374–387. 5. Costa LJ, et al. Leukemia. 2025;39(3):543–554.

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