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on multiple myeloma

Optimising T-cell immunotherapy in patients with multiple myeloma: practical considerations from the European Myeloma Network

The Lancet Haematology, 2025 August; 12(8):e635–49

Comparison of standard-of-care idecabtagene vicleucel and ciltacabtagene autoleucel in relapsed/refractory multiple myeloma

Journal of Clinical Oncology, 2025 May; 43(13):1597–609

Long-term (≥5-year) remission and survival after treatment with ciltacabtagene autoleucel in CARTITUDE-1 patients with relapsed/refractory multiple myeloma

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Anti-GPRC5D CAR T-cell therapy as a salvage treatment in patients with progressive multiple myeloma after anti-BCMA CAR T-cell therapy: a single-centre, single-arm, phase 2 trial

The Lancet Haematology, 2025 May; 12(5):e365–75

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Editor
Catherine Harris Booth

Consulting Editor
Niels van de Donk, MD PhD
Professor of Haematology,
Cancer Center Amsterdam,
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Medical Writers (this issue)
Claire Beveridge
Derek Collett

Art Design
Jan van Halm

Layout and Printing
Drukmeesters,
Zwijndrecht, the Netherlands

Publishing Director
Evelien Enter

Publisher
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Framingham bv
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OPTIMISING T-CELL IMMUNOTHERAPY IN PATIENTS WITH MULTIPLE MYELOMA:

PRACTICAL CONSIDERATIONS FROM THE EUROPEAN MYELOMA NETWORK

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AUTHORS: van de Donk NW, Moreau P, San-Miguel JF, et al., on behalf of the EMN Guidelines Committee
CENTRE FOR CORRESPONDENCE: Department of Hematology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands

BACKGROUND & AIM: Over the last 5 years, the introduction of novel T-cell immunotherapies in the form of chimeric antigen receptor (CAR) T-cell therapies and T-cell redirecting bispecific antibodies (BsAbs) has changed the treatment landscape for patients with relapsed or refractory multiple myeloma, and their potential in earlier lines of treatment is being investigated. The aim of this review was to summarize European Myeloma Network recommendations for optimizing the efficacy and safety of T-cell immunotherapies.

ARTICLE TYPE: Guidelines.

FINDINGS: While the sequential use of different T-cell immunotherapies is feasible in patients who are eligible for both CAR T-cell therapy and BsAbs, treatment with CAR T-cell therapy (preferably cilta-cel) first has been shown to be important for efficacy due to high response rates, durable progression-free survival and improvements in quality of life. Several studies have reported that the response duration to CAR T-cell therapy is substantially decreased in patients who have previously received B-cell maturation antigen (BCMA)-directed BsAb therapy. In addition, there is emerging evidence that relapse after CAR T-cell therapy can be managed effectively with BsAbs. There is also evidence that the sequential use of BsAbs targeting different antigens is possible (although the activity of the second BsAb is usually lower than that of the first) and that sequential BCMA-directed CAR T-cell therapy can achieve durable remission if a different CAR T-cell product is used; retreatment with the same product is not effective.

Timely referral and treatment planning are crucial before initiating T-cell immunotherapy. All candidates should be tested for infectious diseases (e.g. hepatitis B, hepatitis C, HIV), and pulmonary and cardiac testing should be considered for older patients. Modifiable outcomes should be identified and addressed to optimize clinical outcomes. Furthermore, patients receiving T-cell immunotherapy require supportive care to prevent non-relapse mortality. Use of CAR T-cell therapy early in the disease course may reduce the risk of adverse events and is more effective, while early use of BsAbs (in eligible patients) is associated with increased depth of response and longer duration of remission. For bridging therapy, use of drugs that the patient has not already been exposed to is recommended, as is avoiding BCMA-directed agents.

CONCLUSION: Early referral and treatment planning, evaluating modifiable outcomes and choosing an appropriate treatment sequence can improve the efficacy and safety of T-cell immunotherapies.

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COMPARISON OF STANDARD-OF-CARE IDECABTAGENE VICLEUCEL AND CILTACABTAGENE AUTOLEUCEL IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

Journal of Clinical Oncology, 2025 May; 43(13):1597–609

AUTHORS: Hansen DK, Peres LC, Dima D, et al., on behalf of the US Multiple Myeloma Immunotherapy Consortium
CENTRE FOR CORRESPONDENCE: H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA

BACKGROUND & AIM: Idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) are both B-cell maturation antigen-directed chimeric antigen receptor T-cell therapies that are approved for the treatment of relapsed or refractory multiple myeloma (RRMM). The two therapies have not been directly compared in head-to-head trials, meaning there are limited data on which physicians can base treatment selection. In the absence of a randomized controlled clinical trial, the aim of this study was to indirectly compare the efficacy and safety of ide-cel and cilta-cel in patients with RRMM.

STUDY DESIGN: Multicentre, retrospective study.

ENDPOINTS: Response rate; progression-free and overall survival; non-relapse mortality; safety.

METHOD: Data were obtained on patients with RRMM who underwent leukapheresis at one of 19 US academic medical centres with the intention of manufacturing ide-cel or cilta-cel. Inverse probability of treatment weighting was used to balance confounders among patients treated with cilta-cel (n=236) and ide-cel (n=350), and regression analyses were used to compare outcomes according to the therapy received.

RESULTS: The median follow-up was 12.6 months for patients infused with ide-cel and 13.0 months for those receiving cilta-cel. Patient characteristics were well balanced following inverse probability of treatment weighting. Efficacy was better with cilta-cel versus ide-cel, with increased odds of a complete response or better (odds ratio 2.42, 95% confidence interval 1.63–3.60; p<0.001), longer progression-free survival (hazard ratio 0.48, 95% CI 0.36–0.63; p<0.001) and longer overall survival (HR 0.67, 95% CI 0.46–0.97; p=0.03). Compared with patients receiving ide-cel, those treated with cilta-cel were significantly more likely to experience severe (grade ≥3) cytokine release syndrome (OR 6.80, 95% CI 2.28–20.33), delayed neurotoxicity (OR 20.07, 95% CI 4.46–90.20) and infections (OR 2.03, 95% CI 1.41–2.92; p<0.001 for all), and also had higher (although non-statistically significant) likelihoods of any second primary malignancy (OR 1.77, 95% CI 0.89–3.56) and any second primary malignancy excluding non-melanoma skin cancer (OR 1.72, 95% CI 0.74–3.97). There were no associations between therapy type and immune effector cell-associated neurotoxicity syndrome, any-grade cytokine release syndrome, severe cytopenia at days 30 and 90 or non-relapse mortality.

CONCLUSION: This indirect comparison found that cilta-cel was associated with better efficacy and longer survival than ide-cel in patients with RRMM, but with a higher incidence of some toxicities.

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LONG-TERM (≥5-YEAR) REMISSION AND SURVIVAL AFTER TREATMENT WITH CILTACABTAGENE AUTOLEUCEL IN CARTITUDE-1 PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Journal of Clinical Oncology, 2025 September; 43(25):2766–71

AUTHORS: Jagannath S, Martin TG, Lin Y, et al.
CENTRE FOR CORRESPONDENCE: Icahn School of Medicine at Mount Sinai, New York, New York, USA

BACKGROUND & AIM: In the phase 1b/2 CARTITUDE-1 trial, patients with heavily pretreated relapsed or refractory multiple myeloma (RRMM) had deep and durable responses following treatment with ciltacabtagene autoleucel (cilta-cel), a B-cell maturation antigen-directed chimeric antigen receptor (CAR) T-cell therapy. The aim of this analysis was to gain further insights into the characteristics of patients who experienced long-term (≥5 years) clinical benefits after cilta-cel infusion.

STUDY DESIGN: Exploratory post hoc analysis of a multicentre, open-label, phase 1b/2 trial.

ENDPOINTS: Overall survival; progression-free survival rate at 5 years or longer; associated biomarkers (immune cell phenotypes and serum biomarkers); safety.

METHOD: In CARTITUDE-1, adults with RRMM (n=97) who had received at least three previous lines of therapy received a single cilta-cel infusion and were invited to enrol in a 15-year postinfusion follow-up study with evaluations per local standard of care. This analysis compared the characteristics of patients who were progression-free for at least 5 years after infusion versus those with progressive disease.

RESULTS: At a median follow-up of 61.3 months, median overall survival among the 97 treated patients was 60.7 months. A total of 32 patients (33%) were progression-free for at least 5 years without maintenance treatment, of whom 31 (96.9%) had experienced a stringent complete response to cilta-cel. Among these 31 patients, 12 were serially assessed at a single centre and all were both minimal residual disease-negative ($\geq 10^{-5}$ threshold) and imaging-negative at year 5 or later, suggesting potential cure. A further 46 patients (47%) had progressive disease within 5 years. Baseline characteristics were generally comparable between patients with and without progressive disease. Compared with patients with progressive disease within 5 years, those who were progression-free had a higher effector-to-target ratio at peak expansion (p=0.008) and greater CAR+ T-cell expansion (p=0.028); higher baseline levels of haemoglobin (p=0.001) and platelets (p=0.049); a lower neutrophil-over-leukocyte ratio (p=0.03) and higher T-cell-to-neutrophil ratio (p=0.05) at the time of apheresis; and higher proportions of CAR-positive naive T cells in the drug product (p=0.003). The safety profile of cilta-cel was consistent with previous reports.

CONCLUSION: One-third of adults with heavily pretreated RRMM were progression-free and did not require treatment for at least 5 years after receiving cilta-cel.

https://doi.org/10.1200/JCO-25-00760

ANTI-GPRC5D CAR T-CELL THERAPY AS A SALVAGE TREATMENT IN PATIENTS WITH PROGRESSIVE MULTIPLE MYELOMA AFTER ANTI-BCMA CAR T-CELL THERAPY:

A SINGLE-CENTRE, SINGLE-ARM, PHASE 2 TRIAL

The Lancet Haematology, 2025 May; 12(5):e365–75

AUTHORS: Xia J, Sun Q, Zhou D, et al.
CENTRE FOR CORRESPONDENCE: Department of Hematology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, China

BACKGROUND & AIM: GPRC5D (G protein-coupled receptor class C group 5 member D) is expressed primarily on the surface of myeloma cells independently of anti-B-cell maturation antigen (BCMA), and anti-GPRC5D chimeric antigen receptor (CAR) T-cell therapy may have clinical activity in patients with relapsed or refractory multiple myeloma (RRMM) after anti-BCMA CAR T-cell therapy. The aim of this study was to investigate the safety and activity of anti-GPRC5D CAR T cells in patients with MM whose disease has progressed after anti-BCMA CAR T-cell therapy.

STUDY DESIGN: Single-centre, single-arm, open-label, phase 2 trial.

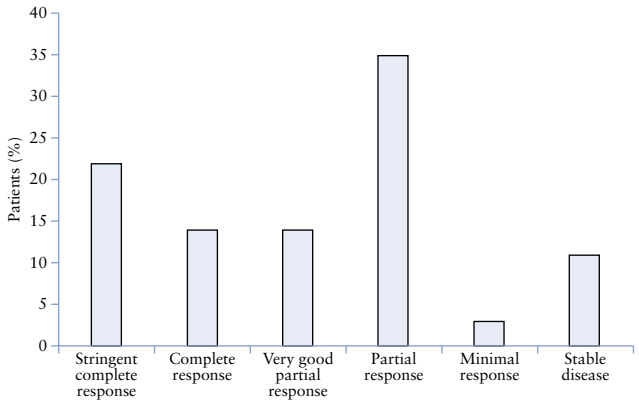
ENDPOINT: Primary: overall response rate. Secondary endpoints included progression-free survival and safety.

METHOD: Adults (n=37) with RRMM whose disease had progressed after anti-BCMA CAR T-cell therapy underwent lymphodepletion followed by a single dose of anti-GPRC5D CAR T cells (2×10^6 cells/kg). Activity was assessed on posttreatment days 14 and 28, at 2, 3, 6 and 12 months, and regularly thereafter, until withdrawal of consent or death.

RESULTS: At a median follow-up of 12.6 months (interquartile range 8.2–20.8 months), the overall response rate was 84% (31/37 patients; Figure). The median time to first response was 0.5 months (IQR 0.5–1.0 months) and the median time to best response was 1.0 months (IQR 0.5–3.0 months). Median progression-free survival was 4.5 months overall and not reached in patients with a complete response or better. Of the 31 patients with a response to therapy, 48% experienced disease progression. All patients had grade 3/4 haematological adverse events, most commonly lymphopenia (97%), leukopenia (92%) and neutropenia (78%). Cytokine release syndrome occurred in 70% of patients and was mostly grade 1/2 (grade 3 in two patients). No deaths were considered to be treatment-related.

CONCLUSION: Patients with RRMM after anti-BCMA CAR T-cell therapy had a high response rate to a single infusion of anti-GPRC5D CAR T cells, with a manageable safety profile.

Response rates (n=37)



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