FraminGHam

on multiple myeloma

Impact of COVID-19 on outcomes with teclistamab in patients with relapsed/refractory multiple myeloma in the phase 1/2 MajesTEC-1 study

Blood Cancer Journal, 2024 October 21; 14(1):186

Phase I trial of MCARH109, a G protein-coupled receptor class C group 5 member D (GPRC5D)-targeted chimeric antigen receptor T-cell therapy for multiple myeloma: an updated analysis

Journal of Clinical Oncology, 2025 February 10; 43(5):498–504

Linvoseltamab for treatment of relapsed/refractory multiple myeloma

Journal of Clinical Oncology, 2024 August 1; 42(22):2702–12

Talquetamab plus teclistamab in relapsed or refractory multiple myeloma

The New England Journal of Medicine, 2025 January 9; 392(2):138–49

ISSUE 2, 2025

CURRENT TITLES

Framingham *on amyloidosis*

Framingham *on atherosclerosis*

Framingham *on benign haematology*

Framingham *on chronic lymphocytic leukaemia*

Framingham *on cystic fibrosis*

Framingham *on dermatology*

Framingham *on diabetes*

Framingham *on endocrinology*

Framingham *on gastroenterology*

Framingham *on gynaecology*

Framingham *on haematological malignancies*

Framingham *on HIV/AIDS*

Framingham *on infectious diseases*

Framingham *on lung cancer*

Framingham *on menopause*

Framingham *on neurology*

Framingham *on respiratory diseases / asthma*

Framingham *on systemic fungal infections*

and many more...

DISCLAIMER

ADVISORY BOARD

OUR PURPOSE

The Framingham series of publications is designed to meet clinical specialists' need for a reliable guide to the most important articles appearing in their field.
Each issue presents an authoritative selection from the recently published literature, with the emphasis on evidence-based medicine. Articles are recommended for inclusion by Framingham's editorial office and an advisory board headed by key opinion leaders in the relevant clinical area.
Framingham's team of medical writers prepares original abstracts of these articles, in a structured format that presents the main points at a glance. Our aim is to convey the essence of each article in a concise but readable style.
Issues are published every three to six months.

Framingham

Editor
Catherine Harris Booth

Consulting Editor
Niels van de Donk, MD PhD
Professor of Haematology,
Cancer Center Amsterdam,
Amsterdam UMC,
Location VU University Medical Center,
Amsterdam, the Netherlands

Medical Writers (this issue)
Milena Braga-Basaria
Derek Collett
David Newton

Art Design
Jan van Halm

Layout and Printing
Drukmeesters,
Zwijndrecht, the Netherlands

Publishing Director
Evelien Enter

Publisher
Waldemar H.G. Dobrowolski

Framingham bv
Postbus 1593
1200 BN Hilversum
The Netherlands
www.framinghampublishers.com

Framingham *on multiple myeloma*
is published by the support of
Sanofi AB
Stockholm, Sweden
MAT-BE-2500655 (ver. 1) Jun 2025

IMPACT OF COVID-19 ON OUTCOMES WITH TECLISTAMAB IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA IN THE PHASE 1/2 MAJESTEC-1 STUDY

Blood Cancer Journal, 2024 October 21; 14(1):186

AUTHORS: van de Donk NW, Bahlis N, Costa LJ, Mateos MV, Nooka AK, Perrot A, Garfall AL, Thaman P, Qi K, Uhlar C, Chastain K, Doyle M, Usmani SZ
CENTRE FOR CORRESPONDENCE: Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands

BACKGROUND & AIM: The phase 1/2 MajesTEC-1 study was designed to assess the use of teclistamab, a B-cell maturation antigen bispecific antibody, in the treatment of patients with triple-class-exposed relapsed or refractory multiple myeloma (RRMM). The enrolment period overlapped with the period of peak infection and death during the COVID-19 pandemic. RRMM is associated with a particularly high risk of infection, and MajesTEC-1 participants had many of the features identified as risk factors for COVID-19 morbidity and mortality. The aim of this analysis was to determine the impact of COVID-19 on the outcomes of patients treated with teclistamab in MajesTEC-1.

STUDY DESIGN: Post hoc analysis of a phase 1/2 study.

ENDPOINTS: Progression-free survival; overall survival; duration of response.

METHOD: In MajesTEC-1, patients with RRMM following at least three lines of therapy (*n*=165) were treated with the recommended phase 2 dose of teclistamab (1.5 mg/kg per week). Precautions to limit infection risk were in place and evolved over time with additional data and experience, and any infections contracted (including COVID-19) were managed according to institutional guidelines. Influenza and COVID-19 vaccination was recommended when available. The median follow-up was 22.8 months, and outcomes were analysed overall, in patients with a complete response or better, by the number of previous lines of therapy, and in the phase 2 efficacy population.

RESULTS: A total of 48 patients (29.1%) had a COVID-19 infection during the study, which resulted in treatment interruption in 29 patients and death in 18 (10.9%). Four of the COVID-19 deaths were considered to be related to teclistamab treatment. In the overall study population, median progression-free survival was 11.3 months, median overall survival was 21.9 months and median duration of response was 21.6 months. The outcomes were better when censored for COVID-19 deaths, at 15.1, 28.3 and 26.7 months, respectively. A similar trend towards improved survival and duration of response after censoring for COVID-19 deaths was seen in all subgroups evaluated.

CONCLUSION: These findings illustrate the impact of COVID-19 on heavily pretreated patients with RRMM at the start of the pandemic, and highlight the importance of infection prevention, monitoring and management in optimizing outcomes in this population.

https://doi.org/10.1038/s41408-024-01160-1

PHASE I TRIAL OF MCARH109, A G PROTEIN-COUPLED RECEPTOR CLASS C GROUP 5 MEMBER D (GPRC5D)-TARGETED CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY FOR MULTIPLE MYELOMA:

AN UPDATED ANALYSIS

Journal of Clinical Oncology, 2025 February 10; 43(5):498–504

AUTHORS: Jurgens EM, Firestone RS, Chaudhari J, Hosszu K, Devlin SM, Shah UA, Landa J, McAvoy DP, Lesokhin AM, Korde N, Hassoun H, Tan CR, Hultcrantz M, Shah GL, Landau HJ, Chung DJ, Scordo M, Eren OC, Dogan A, Giralt SA, Park JH, Rivière I, Brentjens RJ, Smith EL, Wang X, Usmani SZ, Mailankody S
CENTRE FOR CORRESPONDENCE: Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA

BACKGROUND & AIM: Chimeric antigen receptor (CAR) T-cell therapy is an effective treatment for patients with relapsed or refractory multiple myeloma (RRMM), but most patients ultimately relapse on the currently approved agents, which target B-cell maturation antigen (BCMA). MCARH109 is a first-in-class CAR T-cell therapy that targets an alternative myeloma antigen, GPRC5D (G-protein-coupled receptor, class C, group 5, member D). The aim of this study was to investigate responses, toxicities and immune profiles in patients with RRMM receiving MCARH109.

STUDY DESIGN: Open-label, dose-escalation, phase 1 trial.

ENDPOINTS: Primary: safety. Secondary endpoints included response and bone marrow measurable residual disease-negativity. Exploratory endpoints included myeloma cell GPRC5D expression and immune profiles.

METHOD: The study included 17 patients with RRMM, of whom 10 had previously received BCMA-targeted CAR T-cell therapy and two had previously received bispecific antibody therapy. The patients were treated with MCARH109 at one of four dose levels: 25×10^6 (n=3), 50×10^6 (n=3), 150×10^6 (n=6) or 450×10^6 (n=5) CAR T cells. Myeloma cell GPRC5D expression was measured by immunohistochemistry, and immune profiles were examined using high-dimensional spectral flow cytometry.

RESULTS: Over a median follow-up of 37 months (interquartile range 34–39 months), on-target, off-tumour GPRC5D-related toxicities included nail changes in 11 patients, rash in three and dysgeusia in three; all were grade 1 and resolved in most patients. Two patients on the highest dose experienced grade 3 neurotoxicity, which was stable but persistent at last follow-up. The maximum tolerated dose was 150×10^6 CAR T cells. Twelve patients (71%) experienced a partial response or better, including seven who had previously received BCMA-targeted therapy, and the median duration of response was 8.6 months. Eight of the responders were negative for measurable residual disease. Possible GPRC5D loss was seen in six out of 10 MCARH109 responders at relapse, and response to MCARH109 was associated with an activated T-cell phenotype at apheresis.

CONCLUSION: MCARH109 was found to be safe and efficacious at doses of up to 150×10^6 CAR T cells in patients with RRMM, with durable responses and no new toxicities.

https://doi.org/10.1200/JCO-24-01785

LINVOSELTAMAB FOR TREATMENT OF RELAPSED/REFRACTORY MULTIPLE MYELOMA

Journal of Clinical Oncology, 2024 August 1; 42(22):2702–12

AUTHORS: Bumma N, Richter J, Jagannath S, et al.
CENTRE FOR CORRESPONDENCE: Emory University School of Medicine, Atlanta, Georgia, USA

BACKGROUND & AIM: Multiple myeloma often becomes refractory to the three main classes of treatment. Therefore, treatments that use different mechanisms of action and induce deep, durable remission are required. Linvoseltamab is a fully human B-cell maturation antigen × CD3 bispecific antibody that has shown promising antitumour activity in preclinical studies. The aim of this study was to assess the efficacy and safety of linvoseltamab in patients with relapsed or refractory multiple myeloma.

STUDY DESIGN: International, open-label, first-in-human, phase 2 trial.

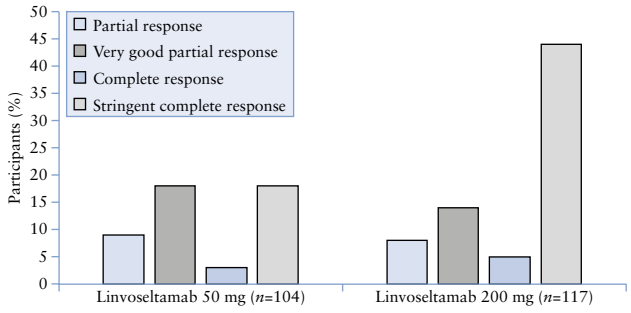
ENDPOINTS: Primary: overall response rate. Secondary: complete response rate; duration of response; progression-free survival; overall survival; safety.

METHOD: Adults with relapsed or refractory multiple myeloma that had progressed on/after or was refractory to at least three lines of therapy, including a proteasome inhibitor, immunomodulatory drug and anti-CD38 antibody, received linvoseltamab 50 mg (*n*=104) or 200 mg (*n*=117) once weekly to week 14, then every 2/4 weeks.

RESULTS: Over a median follow-up of 14.3 months, patients treated with the 200 mg dose had an overall response rate of 70.9% (Figure). The median duration of response was 29.4 months, median progression-free survival was not reached and median overall survival was 31.4 months. Over a median follow-up of 7.4 months, patients treated at the 50 mg dose had an overall response rate of 48.1% (Figure). Rates of treatment-emergent adverse events were similar between dosages except for neutropenia, which occurred more frequently with 200 mg linvoseltamab (42.7% versus 28.8% with 50 mg). Overall, 73.5% of patients treated at 200 mg had grade 3/4 treatment-emergent adverse events and 18.8% discontinued treatment because of treatment-emergent adverse events, mostly infections (9.4%). Immune effector cell-associated neurotoxicity syndrome occurred in 7.7% of patients at this dose. Infections were reported for 74.4% of patients treated at 200 mg, but their frequency and severity lessened over time.

CONCLUSION: In patients with relapsed or refractory multiple myeloma, 200 mg linvoseltamab had high efficacy with acceptable safety.

Overall response to linvoseltamab



https://doi.org/10.1200/JCO.24.01008

TALQUETAMAB PLUS TECLISTAMAB IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA

The New England Journal of Medicine, 2025 January 9; 392(2):138–49

AUTHORS: Cohen YC, Magen H, Gatt M, Sebag M, Kim K, Min CK, Ocio EM, Yoon SS, Chu MP, Rodríguez-Otero P, Avivi I, Quijano Cardé NA, Kumar A, Krevvata M, Peterson MR, Di Scala L, Scott E, Hilder B, Vanak J, Banerjee A, Oriol A, Morillo D, Mateos MV, on behalf of the RedirecTT-1 Investigators and Study Group
CENTRE FOR CORRESPONDENCE: Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

BACKGROUND & AIM: Patients with relapsed or refractory multiple myeloma (RRMM) with prior exposure to immunomodulatory drugs, proteasome inhibitors and anti-CD38 therapies (i.e. triple-class exposure) have a poor prognosis with standard treatments. It is thought that dual antigen targeting with talquetamab (which targets G-protein-coupled receptor, class C, group 5, member D or GPRC5D) plus teclistamab (an anti-B-cell maturation antigen) may enhance treatment potency, eradicate heterogeneous tumour populations, prevent resistance due to antigen escape and improve response durability. The aim of this study was to report early safety and efficacy results for talquetamab plus teclistamab in patients with RRMM.

STUDY DESIGN: Multicentre, non-randomized, open-label, phase 1b/2 study.

ENDPOINTS: Dose-limiting toxic effects; adverse events; overall response.

METHOD: Patients with RRMM with at least triple-class exposure (*n*=94) received escalating doses of subcutaneous talquetamab plus teclistamab in 28-day cycles to determine the recommended phase 2 regimen. This paper reports early safety and efficacy results from the phase 1 dose-escalation portion of the study.

RESULTS: Dose-limiting toxic effects occurred in three patients (grade 3 oral herpes, grade 3 transaminase elevation and grade 4 thrombocytopenia in one patient each). During a median follow-up of 20.3 months (range 0.5–37.1 months), 90 patients (96%) across all dose levels experienced grade 3/4 adverse events, predominantly haematological (80%). The most common adverse events were cytokine release syndrome, neutropenia, taste changes and non-rash skin reactions. Infection of any grade occurred in 84 patients (89%), with grade 3/4 infection in 60 (64%). Across all dose levels, 73 patients (78%) had a response, including 61% with extramedullary disease, with a median time to first response of 1.8 months (range 0.3–7.7 months). The recommended phase 2 regimen was talquetamab 0.8 mg/kg plus teclistamab 3.0 mg/kg every 2 weeks, which was received by 44 patients. Among these patients, 35 (80%) had a response, with a median time to first response of 1.4 months (range 0.3–5.1 months). The likelihood of maintaining a response at 18 months was 86% with the recommended phase 2 regimen and 77% across all dose levels.

CONCLUSIONS: Among patients with RRMM, combination therapy with teclistamab plus talquetamab showed promising antitumour activity. The safety profile was generally consistent with that seen with the agents used as monotherapies, but the incidence of grade 3/4 infections was higher than with either agent alone.

https://doi.org/10.1056/NEJMoa2406536