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on multiple myeloma

The impact of anti-CD38 monoclonal antibody therapy on stem-cell mobilization yields in patients with newly diagnosed multiple myeloma (NDMM) referred from community and academic oncology practices: single center, real world data 2021–2024

Transplantation and Cellular Therapy, 2025 December; 31(12):1006.e1–11

Uncovering the ultra-frail: a distinct subgroup in non-transplant eligible newly diagnosed patients with multiple myeloma, with an inferior clinical outcome

HemaSphere, 2025 December 8; 9(12):e70268

Safety and efficacy of a dexamethasone-sparing regimen with daratumumab and lenalidomide in patients with frailty and newly diagnosed multiple myeloma (IFM2017-03): a phase 3, open-label, multicentre, randomised, controlled trial

The Lancet Oncology, 2025 October; 26(10):1323–33

Dual targeting of extramedullary myeloma with talquetamab and teclistamab

The New England Journal of Medicine, 2026 January 1; 394(1):51–61

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Consulting Editor
Niels van de Donk, MD PhD
Professor of Haematology,
Cancer Center Amsterdam,
Amsterdam UMC,
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Medical Writers (this issue)
Lorraine Law
Kathy Longley
Kevin West

Art Design
Jan van Halm

Layout and Printing
Drukmeesters,
Zwijndrecht, the Netherlands

Publishing Director
Evelien Enter

Publisher
Waldemar H.G. Dobrowolski

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THE IMPACT OF ANTI-CD38 MONOCLONAL ANTIBODY THERAPY ON STEM-CELL MOBILIZATION YIELDS IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM) REFERRED FROM COMMUNITY AND ACADEMIC ONCOLOGY PRACTICES:

SINGLE CENTER, REAL WORLD DATA 2021–2024

Transplantation and Cellular Therapy, 2025 December; 31(12):1006.e1–11

AUTHORS: Uzun D, Paul JM, Jensen A, Tamaresis J, Domingo W, Arai S, Ventura FA, Rocha J, Bennett L, Jones A, Bharadwaj S, Johnston L, Lowsky R, Rezvani A, Shiraz P, Shizuru J, Weng WK, Hosoya H, Sidana S, Miklos D, Muffly L, Mikkilineni L

CENTRE FOR CORRESPONDENCE: Division of Blood and Marrow Transplant and Cellular Therapy, Stanford University School of Medicine, Stanford, California, USA

BACKGROUND & AIM: The inclusion of CD38 monoclonal antibodies (mAbs) in autologous stem-cell transplantation (ASCT) induction regimens has been associated with more patients with newly diagnosed multiple myeloma (NDMM) achieving deeper responses and higher rates of minimal residual disease-negativity. However, the impact of CD38 mAbs on haemopoietic stem-cell mobilization remains unclear, with some clinical trials reporting reduced stem-cell yields and increased plerixafor use following CD38 mAb induction therapy and real-world analyses reporting conflicting results. The aim of this study was to analyse the impact of CD38 mAb-based induction on total stem-cell yield in patients with NDMM undergoing ASCT in a real-world setting.

STUDY DESIGN: Retrospective single-centre study.

ENDPOINTS: Total stem-cell yield per apheresis session; plerixafor use; number of apheresis sessions; cost differences.

METHOD: Data were retrieved on patients with NDMM referred for ASCT who received induction therapy with either CD38 mAb-containing triplet/quadruplet therapy (n=172) or non-CD38-based triplet therapy (n=203), followed by stem-cell mobilization with granulocyte-colony stimulating factor with or without plerixafor. The stem-cell collection target was ≥2×10^6 CD34$^+$ cells/kg, with another 2×10^6 CD34$^+$ cells/kg required as backup. Independent predictors of stem-cell yield were assessed using multivariable linear regression models, and a cost analysis was performed.

RESULTS: Compared with patients receiving non-CD38-based induction therapy, those receiving CD38 mAb-containing induction therapy had a significantly lower (though clinically comparable) median total stem-cell yield (5.2 versus 5.5×10^6 CD34$^+$ cells/kg; p=0.001), and required a higher number of apheresis sessions (median 2 versus 1 session; p=0.0008) and more doses of plerixafor (median 2 versus 1 dose; p=0.0003) to achieve the stem-cell collection target. Multivariable analysis found that the average stem-cell yield significantly decreased by 9.4% with exposure to CD38 mAb (p<0.05) and by 18.9% with each additional day of apheresis (p<0.001), and increased by 3.4% with each additional week of post-induction washout (p=0.015). In the cost analysis, stem-cell mobilization cost $23,285 more in the CD38 mAb-exposed patient group.

CONCLUSION: In this real-world analysis, CD38 mAb-containing ASCT induction was associated with a reduced stem-cell mobilization yield and required roughly twice as many apheresis sessions and plerixafor doses to reach the minimum stem-cell threshold for ASCT, leading to higher stem-cell mobilization costs.

https://doi.org/10.1016/j.jtct.2025.08.014

UNCOVERING THE ULTRA-FRAIL: A DISTINCT SUBGROUP IN NON-TRANSPLANT ELIGIBLE NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA, WITH AN INFERIOR CLINICAL OUTCOME

HemaSphere, 2025 December 8; 9(12):e70268

AUTHORS: Groen K, Smits F, Nasserinejad K, et al.
CENTRE FOR CORRESPONDENCE: Department of Hematology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands

BACKGROUND & AIM: Clinical characteristics and outcomes can differ markedly in patients with non-transplant-eligible newly diagnosed multiple myeloma (NTE-NDMM) according to frailty. Three frailty subgroups have been proposed: frail-by-age-alone (>80 years, no comorbidities or impairments in activities of daily living); frail-by-impairments (≤80 years, with comorbidities and/or impairments in activities of daily living); and ultra-frail (>80 years, with comorbidities and/or impairments in activities of daily living). The aim of this study was to examine the impact of frailty subtype on overall survival (OS) in a large group of patients with NTE-NDMM.

STUDY DESIGN: Analysis of pooled data from two prospective trials (HOVON-123 and HOVON-143).

ENDPOINTS: Progression-free survival (PFS); second PFS (PFS2); OS.

METHOD: The analysis included 202 frail patients with NTE-NDMM, of whom 33 were frail-by-age-alone, 94 were frail-by-impairments and 75 were ultra-frail. Cox proportional hazard models were used to compare survival outcomes between the three groups. To account for potential confounding factors, the results were corrected for baseline disease characteristics identified as significant predictors for survival outcomes in multivariable analysis.

RESULTS: Median PFS was 12.7 months in the ultra-frail group, 16.5 months in the frail-by-impairments group and 21.2 months in the frail-by-age-alone group. The strongest predictor for PFS was a composite of lactate dehydrogenase, β2-microglobulin (β2M) and albumin levels, and median PFS did not differ significantly between the three subgroups after adjustment for these factors. Ultra-frail patients had significantly shorter median PFS2 compared with frail-by-impairments and frail-by-age-alone patients (22.4 versus 31.4 and 40.0 months). After adjustment for β2M levels (the strongest predictor for PFS2), PFS2 remained significantly shorter in ultra-frail versus frail-by-impairments patients (hazard ratio 1.19, 95% confidence interval 1.01–1.41; p=0.04) but not compared with frail-by-age-alone patients. Ultra-frail patients also had significantly shorter median OS compared with both frail-by-impairments and frail-by-age-alone patients (23.7 versus 38.2 and 49.0 months). After adjustment for β2M and albumin levels (the strongest predictors for OS), OS remained significantly shorter in ultra-frail versus both frail-by-impairments (HR 1.28, 95% CI 1.07–1.52; p<0.01) and frail-by-age-alone patients (HR 1.92, 95% CI 1.14–3.22; p=0.01).

CONCLUSION: Among patients with NTE-NDMM, those classified as ultra-frail had inferior OS versus those categorized as frail-by-impairments and frail-by-age-alone.

https://doi.org/10.1002/hem3.70268

SAFETY AND EFFICACY OF A DEXAMETHASONE-SPARING REGIMEN WITH DARATUMUMAB AND LENALIDOMIDE IN PATIENTS WITH FRAILTY AND NEWLY DIAGNOSED MULTIPLE MYELOMA (IFM2017-03):

A PHASE 3, OPEN-LABEL, MULTICENTRE, RANDOMISED, CONTROLLED TRIAL

The Lancet Oncology, 2025 October; 26(10):1323–33

AUTHORS: Manier S, Lambert J, Hulin C, et al.
CENTRE FOR CORRESPONDENCE: Department of Hematology, University Hospital of Lille, Lille, France

BACKGROUND & AIM: Elderly, frail patients with multiple myeloma have a lower tolerance of standard treatment with lenalidomide and dexamethasone and worse outcomes than younger, fitter patients, in part because of dexamethasone toxicity. The aim of this study was to compare the efficacy and safety of a dexamethasone-sparing regimen based on lenalidomide and daratumumab versus standard lenalidomide and dexamethasone in frail patients with multiple myeloma.

STUDY DESIGN: Prospective, randomized controlled, phase 3 trial.

ENDPOINTS: Primary: progression-free survival. Secondary endpoints included treatment response, overall survival and adverse events.

METHOD: The study involved 295 patients aged ≥65 years (median 81 years, 61% ≥80 years) with multiple myeloma and an Eastern Cooperative Oncology Group proxy frailty score ≥2. Of the 295, 200 were randomized to lenalidomide (25 mg/day orally on days 1–21 of each 28-day cycle) plus daratumumab (1800 mg subcutaneously every 1–4 weeks on a decreasing schedule). Dexamethasone (20 mg orally weekly) was administered during the first two cycles only (dexamethasone-sparing group). The other 95 patients received the same lenalidomide dosage plus dexamethasone (20 mg weekly; control group). Treatment was continued until disease progression or unacceptable toxicity.

RESULTS: Patients were followed for a median of 46.3 months (interquartile range 46.0–52.7 months). The estimated median progression-free survival was 53.4 months in the dexamethasone-sparing group and 22.5 months in the control group (hazard ratio 0.51, 95% confidence interval 0.37–0.70; $p<0.0001$). The overall response rate was 92% and 85%, respectively. Moreover, 32% of patients in the dexamethasone-sparing group had a very good partial response or better versus 20% in the control group ($p=0.044$), indicating that dexamethasone-sparing did not compromise responses. Median overall survival was not reached in the dexamethasone-sparing group versus 47.3 months in the control group (HR 0.52, 95% CI 0.35–0.77; $p=0.0001$). The most common grade 3–5 adverse events in the dexamethasone-sparing and control groups were neutropenia (55% versus 24%, respectively) and infection (19% versus 21%); 63% and 69%, respectively, had at least one serious adverse event, which led to death in 12% (23/200) and 13% (12/95). In addition, 2% of patients in each group had treatment-related adverse events.

CONCLUSION: In elderly, frail patients with multiple myeloma, treatment with a dexamethasone-sparing regimen based on lenalidomide and daratumumab was associated with significantly longer progression-free survival than the standard lenalidomide and dexamethasone regimen.

https://doi.org/10.1016/S1470-2045(25)00280-3

DUAL TARGETING OF EXTRAMEDULLARY MYELOMA WITH TALQUETAMAB AND TECLISTAMAB

The New England Journal of Medicine, 2026 January 1; 394(1):51–61

AUTHORS: Kumar S, Mateos MV, Ye JC, et al., for the RedirecTT-1 Investigators Study Group
CENTRE FOR CORRESPONDENCE: Mayo Clinic Rochester, Rochester, Minnesota, USA

BACKGROUND & AIM: Individuals with plasmacytomas that are non-contiguous with bone marrow (true extramedullary myeloma) have a high risk of disease progression or relapse. In the phase 1 RedirecTT-1 study, dual-antigen targeting with the anti-GPRC5D (G-protein-coupled receptor, class C, group 5, member D) agent talquetamab plus the anti-B-cell maturation antigen teclistamab led to a greater and more durable response than either agent alone among patients with triple-class-exposed relapsed or refractory multiple myeloma, including true extramedullary myeloma. The aim of this study was to evaluate the efficacy and safety of talquetamab plus teclistamab solely in patients with drug-resistant, true extramedullary myeloma.

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

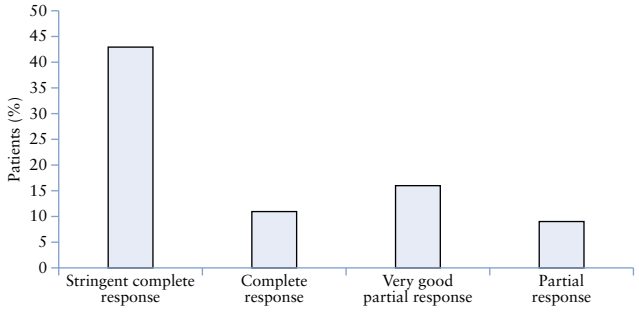
ENDPOINTS: Primary: overall response. Secondary endpoints included duration of response, progression-free survival and overall survival.

METHOD: Adults with drug-resistant true extramedullary myeloma received open-label subcutaneous talquetamab (0.8 mg/kg) plus teclistamab (3.0 mg/kg) every other week in 28-day cycles. Treatment was continued until disease progression, unacceptable toxicity or death.

RESULTS: At the time of the primary analysis, 90 participants had received talquetamab plus teclistamab, with a median follow-up of 12.6 months (range 0.5–19.5 months). The overall response rate was 79%, with a very good partial response or better in 70% and a complete response or better in 54% (Figure). Median duration of response was 13.8 months, with 64% of responses lasting for at least 12 months; 49 patients (54%) were still receiving treatment at the time of the data cut-off. At 12 months, the progression-free survival rate was 61% and the overall survival rate was 74%. Grade 3/4 adverse events occurred in 76% of participants (mostly cytopenias) and there were five treatment-related deaths.

CONCLUSIONS: The majority of these patients with drug-resistant true extramedullary myeloma responded to talquetamab plus teclistamab. However, there was a high incidence of grade 3 or worse adverse events.

Responses among patients with a partial response or better



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