Annals of Clinical and Medical Case Reports

Case Report

ISSN 2639-8109 | Volume 13

Sequential Bispecific Antibodies in Functional and Clinical High Risk Multiple Myeloma, Manifesting with Extramedullary Disease at Relapse: A Case Report

Morè S*, Manieri VM, Corvatta L, Morsia E, Poloni A, and Offidani M

Department of Medicine and Surgery, Marche Polytechnic University, Italy

***Corresponding author:**

Sonia Morè,
Department of Medicine and Surgery, Marche Polytechnic University, Italy

Received: 02 Jan 2024
Accepted: 06 Feb 2024
Published: 12 Feb 2024
J Short Name: ACMCR

Citation:

Morè S, Sequential Bispecific Antibodies in Functional and Clinical High Risk Multiple Myeloma, Manifesting with Extramedullary Disease at Relapse: A Case Report. Ann Clin Med Case Rep. 2024; V13(2): 1-2

Keywords:

Immunomodulatory; Paraskeletal; Orthopaedic; Gammopathy

1. Case Report

Despite recent advances in the treatment of multiple myeloma (MM), the disease remains incurable. Triple class refractory (TCR) patients, defined as refractory to a proteasome inhibitor (PI), immunomodulatory agent (IMiD), and anti-CD38 monoclonal antibody have demonstrated to have especially poor outcomes with a median overall survival of less than 1 year [1-3]. Novel drugs and novel targets have been studied to overcome the dismal prognosis of this group of patients, with great results in terms of response and outcomes by pivotal trials [4-5]. Furthermore, obtaining the same results in real life settings and in particular in functional or clinical high risk diseases [6,7] could be very challenging.

Here we describe a clinical high risk triple class refractory MM patient treated with two sequential bispecific antibodies targeting BCMA and GPRC5D in Italy.

A 59-years old female was referred to us in November 2019 for a diagnosis of IgA kappa MM, after a hospitalization in orthopaedic clinic for a femur fracture, during which severe anemia and monoclonal gammopathy were diagnosed. Her cytogenetic risk was high, but not double hit, having t(14;16) and 1q21 gain. She also had bone involvement with multiple osteolytic lesions and a paraskeletal fleshy lesion of left femur (diam 4 x 3 cm). She did't have clinical high risk features at baseline evaluation, not presenting with extramedullary disease (EMD) or circulating plasma cells. She was treated with bortezomib-thalidomide-dexamethasone triplet induction regimen for four cycles, followed by double autologous stem cells transplants and maintenance therapy with lenalidomide monotherapy. The patient obtained a complete remission, maintained for 12 months. In January 2022, the first relapse occurred at less than 18 months from transplant, configuring the patient as functional high risk. She received a salvage therapy with 13 cycles of carfilzomib-cyclophosphamide-dexamethasone therapy, obtaining a very good partial remission. When she relapsed, in January 2023, she received 5 cycles of isatuximab-pomalidomide-dexamethasone obtaining a stable disease. In July 2023 the patient relapsed again with two extramedullary plasmocytomas in the right scalf (diam 4 x 3 cm) and the interruction of the vertebral cortex in D8 with an initial spinal cord compression, identified by CT scan. A clear bone marrow involvement was lack, being bone marrow plasma cell <10%, and cytogenetic profile remained the same of baseline evaluation, renal failure and initial hypercalcemia occurred. She was triple-refractory with functional and clinical high risk disease characteristics. Teclistamab was available in Named Patient Program (NPP) in Italy and she started this anti-BCMA bispecific antibody in August 2023. Five cycles of Teclistamab were done with palliative Radiotherapy 800 Gy on D8-D11 vertebral tract. She immediately obtained a rapid deep haematological disease response after the inpatient step up doses of the drug, without clinical response of right scalp plasmocytomas which grew up, but she lose her response after the first month. CRS and ICANS were not documented during treatment, despite disease burden. In October 2023 the patient went to the emergency room for fever and hypotension. She was diagnosed with a septic shock without microbiological data except for a CMV reactivation, with resolution after antimicrobial therapy. At the same time she was

diagnosed with a MM relapse in November 2023, with anemia and thrombocytopenia due to massive bone marrow involvement and renal failure. In November 2023 she started anti-GPRC5D bispecific antibody Talquetamab, into a compassionate program use in Italy. She obtained haematological and clinical complete response with the disappearance of her EMD after the first month of therapy. She was diagnosed with grade 2 CRS during step up doses, treated with a single dose of tocilizumab according to guidelines, but no ICANS. Hypogammaglobulinemia <200 mg/dl was detected at the same time with haematological complete remission, without infection signs, and treated with subcutaneous immunoglobulins. Cutaneous grade 1 erythematous adverse event on bilateral legs was diagnosed and treated with local steroid. The patients is going to receive Talquetamab therapy for the third month.

This is an example of differences of novel therapies in clinical trials and in real life settings. Median prior lines of therapy (LOT) of patients enrolled in MagnetisMM-1 trial were 5 (range 2-14), with 78% of triple-class refractory patients, higher than our patients who have received only three lines of therapy becoming triple-refractory very early in her patient journey. Being median progression free survival (PFS) in the trial 12.5 months [8] in a very pre-treated population, and 18.1 months in the subgroup with ≤3 prior LOT [9], we should expect a great outcome in our less pre-treated patient. EMD and clinical/functional high risk characteristics were rare in the trial, being 17% the first and 26% the second, so subgroup analysis were difficult to extrapolate, even if EMD, ISS stage III disease and having ≥60% marrow plasma cells were each associated with lower response rates. Recent real life data of Teclistamab showed significantly lower overall response rate (ORR) and median PFS in patients with EMD (37%/2.1 months), and/or an ISS 3 (37%/1.3 months) [10]. EMD was recently confirmed to be one of the factors associated with inferior PFS in real life MM population [11,12]. Among the studies that reported ORRs in patients with EMD, talquetamab was found to elicit the highest ORR, and the association of teclistamab plus talquetamab was the only combination to report an ORR in patients with EMD relapsed/refractory multiple myeloma [13].

In conclusion, we described a very quick haematological but not EMD disease response, and short duration of it with anti-BCMA bispecific antibody in a TCR patient with clinical high risk disease and only three previous LOTs. Changing target of drugs should be a solution, and an anti-GPRC5D has obtained in this case a deep and quick response also on EMD, that should be confirmed in the future evaluations. Responses and outcomes of functional and clinical high risk MM are worse than overall MM population also with novel therapies. Future studies are urgently needed to better define these subgroups of diseases, possibly by molecular characterization of EMD plasmocytomas, in order to tailor and optimize their treatment strategy.

References

1. Mateos MV, Weisel K, De Stefano V, Goldschmidt H, Delforge M, Mohty M, et al. LocoMMotion: a prospective, non-interventional, multinational study of real-life current standards of care in patients with relapsed and/or refractory multiple myeloma. Leukemia. 2022; 36(5): 1371–6.
2. Gandhi UH, Cornell RF, Lakshman A, Gahvari ZJ, McGehee E, Jagosky MH, et al. Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia. 2019; 33(9): 2266–75.
3. Morè S, Corvatta L, Manieri MV, Olivieri A, Offidani M. Real-world assessment of treatment patterns and outcomes in patients with relapsed-refractory multiple myeloma in an Italian haematological tertiary care centre. Br J Haematol. 2023; 201(3): 432–42.
4. Moreau P, Garfall AL, van de Donk NWCJ, Nahi H, San-Miguel JF, Oriol A, et al. Teclistamab in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2022; 387(6): 495–505.
5. Chari A, Minnema MC, Berdeja JG, Oriol A, van de Donk NWCJ, Rodríguez-Otero P, et al. Talquetamab, a T-Cell–Redirecting GPRC5D Bispecific Antibody for Multiple Myeloma. N Engl J Med [Internet]. 2022; 387(24): 2232–44.
6. Hagen P, Zhang J, Barton K. High-risk disease in newly diagnosed multiple myeloma: beyond the R-ISS and IMWG definitions. Blood Cancer J. 2022; 12(5): 83.
7. Marcon C, Simeon V, Deias P, Facchin G, Corso A, Derudas D, et al. Experts' consensus on the definition and management of high risk multiple myeloma. Front Oncol. 2023; 12: 1096852.
8. van de Donk NWCJ, Moreau P, Garfall AL, Bhutani M, Oriol A, Nooka AK, et al. Long-term follow-up from MajesTEC-1 of teclistamab, a B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma (RRMM). J Clin Oncol [Internet]. 2023; 41(16): 8011.
9. Donk N, Popat R, Rosiol L, Besemer B, Lopez JM, Trancucci D, et al. TECLISTAMAB IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM): MAJESTEC-1 SUBGROUP ANALYSIS BY LINES OF THERAPIES. Hematol Transfus Cell Ther [Internet]. 2023; 45: 397–8.
10. Riedhammer C, Bassermann F, Besemer B, Bewarder M, Brunner F, Carpinteiro A, et al. Real-world analysis of teclistamab in 123 RRMM patients from Germany. Leukemia [Internet]. 2024.
11. Dima D, Davis J, Ahmed N, Sannareddy A, Shaikh H, Mahmoudjafari Z, et al. Real-World Safety and Efficacy of Teclistamab for Patients with Heavily Pretreated Relapsed-Refractory Multiple Myeloma. Blood. 2023; 142: 91.
12. Riedhammer C, Bassermann F, Besemer B, Bewarder M, Brunner F, Carpinteiro A, et al. Real-World Analysis of Teclistamab in 115 RRMM Patients from Germany. Blood [Internet]. 2023; 142: 3329.
13. Vegivinti CTR, Lawrence Alexander Santhi J, Liu L, Keesari PR, Thakur R, Hammami MB, et al. Efficacy of Bispecific Antibodies Vs CAR-T in the Treatment of Extramedullary Disease and High-Risk Cytogenetics in Relapsed Multiple Myeloma: A Systematic Review and Meta-Analysis. Blood [Internet]. 2023; 142(1): 1994.