Dialysis independence for a young patient with refractory multiple myeloma treated with teclistamab: A case report

IOANNIS NTANASIS-STATHOPOULOS[1], ILIAS KATSADOUROS[1], PANAGIOTIS MALANDRAKIS[1], ERASMIA PSIMENOU[1], MELETIOS-ATHANASIOS DIMOPOULOS[1,2] and MARIA GAVRIATOPOULOU[1]

[1]Plasma Cell Dyscrasias Unit, Department of Clinical Therapeutics, Alexandra General Hospital, School of Medicine, National and Kapodistrian University of Athens, 11528 Athens, Greece; [2]Department of Medicine, Korea University, Seoul 02841, Republic of Korea

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Abstract. Teclistamab, a B-cell maturation antigen-targeting bispecific antibody, offers a promising treatment option for relapsed/refractory multiple myeloma (RRMM), even in patients with severe renal impairment. The present study describes the case of a 47-year-old woman with RRMM who achieved minimal residual disease negativity and dialysis independence following teclistamab treatment. Despite prior resistance to multiple therapies, including an anti-CD38 monoclonal antibody (daratumumab), two proteasome inhibitors (bortezomib and carfilzomib), an immunomodulatory drug (lenalidomide), an exportin 1 inhibitor (selinexor), a BCL-2 inhibitor (venetoclax) and dexamethasone, and post-autologous stem cell transplantation relapse, teclistamab induced a deep hematological response. Cytokine release syndrome was manageable and no major complications occurred. The present case highlights the feasibility and effectiveness of teclistamab in patients with end-stage renal disease.

Introduction

The landscape of relapsed/refractory myeloma (RRMM) has evolved considerably with the introduction of bispecific antibodies, especially those targeting B-cell maturation antigen (BCMA) (1). In the phase 1/2 MajesTEC-1 clinical trial (2), 165 patients diagnosed with relapsed and/or refractory myeloma were enrolled. All of them were triple-class exposed i.e. they had received at least three prior lines of therapy, including an immunomodulatory drug, a proteasome inhibitor, and an anti-CD38 antibody. Subcutaneous teclistamab was administered weekly at 1.5 mg/kg and the overall response rate reached 65%, whereas minimal residual disease negativity (MRD) rate was 27%, and the median progression-free survival was 11.3 months (2). Following regulatory approval, teclistamab can be administered to patients with characteristics not necessarily identical to the population of the registrational trial (2). Therefore, real-world data are required to determine the safety and efficacy in patients with comorbidities. Herein, we present the case of a patient with RRMM, who achieved disease remission and dialysis independence.

Case report

A 47-year-old woman presented at Alexandra General Hospital (Athens, Greece) in November 2022 with a six-month history of worsening back pain and an Eastern Cooperative Oncology Group Performance Status (ECOG PS)2. The patient had anemia (hemoglobin=7 g/dl), acute kidney injury (serum creatinine=3.39 mg/dl, urea=89 mg/dl) and hypercalcemia (corrected calcium=11.9 mg/dl). Serum albumin was 4.2 g/dl, serum total protein was 6.7 g/dl and serum lactate dehydrogenase levels were 200 mg/dl (abnormal). Serum and urine immunofixation were positive for kappa free light chains, whereas serum electrophoresis showed a M-spike of 0.5 g/dl. 24-h urine protein was calculated at 12 g, and urine electrophoresis demonstrated the presence of a U-spike of 11 g/24 h. Serum kappa free light chains levels were 79,504 mg/l and serum lamda free light chain levels were 6.29 mg/dl (kappa/lamda ratio=12,639). The serum β2-microglobulin was 22 mg/l. Whole-body, low-dose computed tomography and whole-body magnetic resonance imaging revealed multiple osteolyses and L2, L4 and L5 fractures. Furthermore, a S2-S5 para-osseous lesion was identified. A bone marrow biopsy showed a 80% infiltration of kappa-restricted monoclonal plasma cells. The fluorescence in situ hybridization cytogenetic testing revealed the presence of translocation t(11;14) (79% of the examined nuclei) and 1q addition (71%). Therefore, the patient was diagnosed with kappa light chain multiple myeloma, stratified as International Stage System (ISS)-3, revised ISS-2, and second revised ISS-3.

Our patient met the eligibility criteria for autologous stem cell transplantation (ASCT). Therefore, she started induction therapy with daratumumab, bortezomib, lenalidomide and

Correspondence to: Dr Maria Gavriatopoulou, Plasma Cell Dyscrasias Unit, Department of Clinical Therapeutics, Alexandra General Hospital, School of Medicine, National and Kapodistrian University of Athens, 80 Vasilissis Sofias Avenue, 11528 Athens, Greece
E-mail: mariagabria@gmail.com; mgavria@med.uoa.gr

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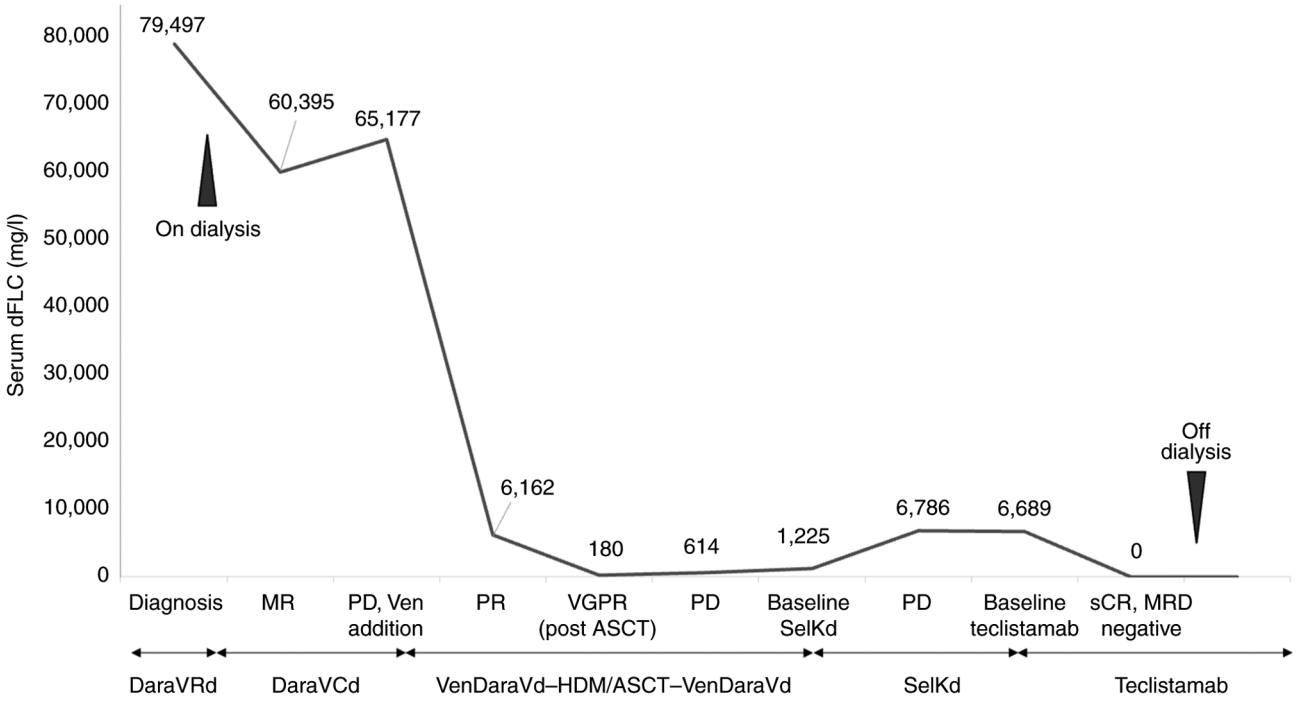

Figure 1. A schematic overview of the succession of treatments and fluctuation of serum dFLC levels during the disease course. FLC, free light chains; MR, minor response; PR, partial response; VGPR, very good partial response; sCR, stringent complete remission; MRD, minimal residual disease; PD, progressive disease; Ven, venetoclax; Dara, daratumumab; V, bortezomib; R, lenalidomide; d, dexamethasone; C, cyclophosphamide; HDM, high dose melphalan; ASCT, autologous stem cell transplant; Sel, selinexor; K, carfilzomib.

dexamethasone (DaraVRd) with a plan for four 28-day cycles, with adjusted lenalidomide dose due to renal impairment. However, creatinine clearance showed a persistent decrease despite the immediate initiation of anti-myeloma treatment, and the patient was put on renal dialysis three times per week due to anuria and acidosis in blood gases, just before the completion of the first cycle of treatment. Lenalidomide was temporarily discontinued and it was replaced by cyclophosphamide (DaraVCd). The patient also reported exacerbating bone pain along with gradual disability in walking and worsening PS=3, despite the daily administration of opioid analgesics and paracetamol. A new imaging revealed imminent spinal cord compression. Therefore, the patient underwent urgent radiotherapy of the S1-S5 area with a total dose of 20 Gy. A stabilization followed by gradual improvement of the bone pain and ability to walk was showed in the following 4 weeks.

Regarding myeloma response after one cycle of DaraVCd, a minor response (MR) was noted; however, a sharp dFLC increase was documented at the end of the second cycle. In view of the new disease progression, and the presence of t(11;14), venetoclax at a target dose of 400 mg was added, whereas cyclophosphamide was interrupted. After two cycles of venetoclax-based treatment, the patient achieved a partial response (PR). The patient then underwent mobilization with cyclophosphamide followed by dose-adjusted melphalan due to renal impairment and ASCT. Despite being on dialysis, there were no major complications. After ASCT, the patient achieved a very good partial response (VGPR) and consolidation with venetoclax, daratumumab, bortezomib and dexamethasone was initiated.

However, after two cycles of consolidation, an increase in dFLC was observed and biochemical disease progression was subsequently confirmed. The combination of selinexor with carfilzomib and dexamethasone was started, but the disease showed no response; instead, the dFLC continued to rise up to 6,688.91 mg/l.

Taking into consideration that our patient with RRMM had an early relapse short after salvage ASCT and she had been refractory to multiple drugs, including two proteasome inhibitors (bortezomib, carfilzomib), one immunomodulatory agent (lenalidomide), an anti-CD38 monoclonal antibody (daratumumab), a BCL-2 inhibitor (venetoclax), an exportin-1 inhibitor (selinexor) and conventional chemotherapy (cyclophosphamide), treatment with teclistamab was initiated. The patient was hospitalized for close monitoring during step-up dosing. After the first dose, cytokine release syndrome (CRS) grade 2 occurred, but it resolved without sequalae with supportive measures and administration of tocilizumab. Importantly, VGPR was achieved at day 15 of the first cycle of treatment. After 4 cycles of treatment with teclistamab, the dFLC, U-spike and M-spike had decreased to zero, whereas both serum and urine immunofixations were negative for monoclonal protein (Fig. 1). Bone marrow aspiration was performed and the patient had negative MRD assessed at the level of $2x10^{-6}$ (Euroflow). Regarding adverse events, subcutaneous immunoglobulin administration was initiated at the start of the third cycle of treatment due to marked hypogammaglobulinemia and frequent upper respiratory tract infections. Furthermore, a gradual improvement in the renal function was observed, which enabled the gradual decrease in the frequency and the duration of dialysis sessions. Eventually, renal dialysis was discontinued after the end of the fourth cycle of treatment with teclistamab. Currently, our patient has a progression-free survival of 16 months on her last treatment, she has no bone

pain even without taking any analgesics, PS=0, she remains MRD negative off dialysis for 12 months with a creatinine clearance of 48 ml/min/1.73 m^2 and continues teclistamab monthly.

Discussion

T-cell engagers and CAR-T cells overall have been demonstrated to be effective and safe in moderate renal failure (3). In the MajesTEC-1 trial the population of patients with chronic renal disease was underrepresented, as 73% of the participants had eGFR >60 ml/min (2). Mild and moderate renal failure do not affect substantially the pharmacokinetic parameters of teclistamab. IgG antibodies, such as teclistamab, are eliminated mainly through intracellular catabolism, as due to their molecular weight are too large to be filtered through renal excretion (4). Therefore, we may support that the effectiveness and safety of teclistamab is not compromised in patients with end-stage renal disease.

Regarding published real-world data, monotherapy with teclistamab in heavily pretreated patients with triple- and penta-refractory multiple myeloma and high-risk disease characteristics results in deep hematological responses comparable to those of the MajesTEC-1 trial. The safety profile pertains mainly to CRS during the first infusions and increased risk for infections (5-9). A large retrospective study by the International Myeloma Working Group included data from 210 patients treated with teclistamab; 26 among them had CrCl <30 ml/min. Although it was a subgroup analysis, the presence of renal impairment did not alter survival outcomes (9). Another retrospective study has reported a non-statistically significant higher incidence of acute kidney injury in patients treated with teclistamab than those receiving CAR-T cell therapy. Nonetheless, it is unclear whether the worsened renal function could be attributed to disease progression or to therapy (10).

One of the limitations of our study pertains to the small sample size; however, our findings are consistent with the available data in the literature. In a case series of 4 patients undergoing hemodialysis, a step-up dosing teclistamab regimen, irrespective of dialysis timing, was initiated successfully with only one patient developing grade 1 CRS (11). In another retrospective study of 13 patients with mostly myeloma-related end-stage kidney disease, teclistamab was safely administered post dialysis. VGPR or better was achieved in all patients with a 4-month median follow up, whereas half of them experienced grade 1 or 2 CRS. In other two studies, 14/15 and 5/7 patients with RRMM and eGFR <30 ml/min responded to teclistamab. CRS grade 1/2 was frequent, whereas patients with extramedullary disease were less likely to respond (12,13), which has been also reported in a larger real-world study (14). It is essential to highlight the need for collaborative efforts to conduct large prospective or even retrospective studies in order to determine precisely the safety and efficacy of teclistamab in this challenging patient population.

Overall, in the lack of prospective studies in the field, our case underlines the feasibility of teclistamab administration in patients with RRMM and severe renal impairment, giving the potential of dialysis independence.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MG and MAD designed the research. INS, IK, PM, EP, MAD and MG performed the research. INS and MG confirm the authenticity of all the raw data. INS and IK wrote the first draft of the paper. PM, EP, MAD and MG revised the draft and provided critical feedback. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Ethics approval for publication was obtained from the Institutional Review Board of Alexandra General Hospital (58/2/21.02.25).

Patient consent for publication

Written informed consent was obtained from the patient.

Competing interests

INS declares honoraria from Janssen. PM declares honoraria from Janssen. MAD declares honoraria from Abbvie, Amgen, Bristol Myers Squibb, GSK, Janssen, Karyopharm, Pharmacyclics Inc, Pfizer, Sanofi, and Takeda. MG declares honoraria from GSK, Janssen, Sanofi, Abbvie, Amgen, and Takeda. The other authors declare that they have no competing interests.

References

1. Kleber M, Ntanasis-Stathopoulos I and Terpos E: BCMA in multiple Myeloma-A promising key to therapy. J Clin Med 10: 4088, 2021.
2. Moreau P, Garfall AL, van de Donk NWCJ, Nahi H, San-Miguel JF, Oriol A, Nooka AK, Martin T, Rosinol L, Chari A, *et al*: Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med 387: 495-505, 2022.
3. Dimopoulos MA, Merlini G, Bridoux F, Leung N, Mikhael J, Harrison SJ, Kastritis E, Garderet L, Gozzetti A, van de Donk NWCJ, *et al*: Management of multiple myeloma-related renal impairment: Recommendations from the International Myeloma Working Group. Lancet Oncol 24: e293-e311, 2023.
4. Ryman JT and Meibohm B: Pharmacokinetics of monoclonal antibodies. CPT Pharmacometrics Syst Pharmacol 6: 576-588, 2017.
5. Mohan M, Monge J, Shah N, Luan D, Forsberg M, Bhatlapenumarthi V, Balev M, Patwari A, Cheruvalath H, Bhutani D, *et al*: Teclistamab in relapsed refractory multiple myeloma: Multi-institutional real-world study. Blood Cancer J 14: 35, 2024.

6. Sandahl TB, Soefje SA, Fonseca R, Ailawadhi S, Parrondo R, Lin D, Wu B, Calay ES, Silvert E, Kim N, *et al*: Real-world safety and health care resource utilization of teclistamab under an outpatient model for Step-Up dosing administration. JCO Oncol Pract 21: 702-709, 2025.
7. Gordon B, Fogel L, Varma G, Saldarriaga MM, Ahn J, Aleman A, Caro J, Chen X, Monge J, Parmar H, *et al*: Teclistamab demonstrates clinical activity in Real-world patients ineligible for the pivotal Majestec-1 trial. Blood 142: 4741-4741, 2023.
8. Dima D, Davis JA, Ahmed N, Jia X, Sannareddy A, Shaikh H, Shune L, Kaur G, Khouri J, Afrough A, *et al*: Safety and efficacy of teclistamab in patients with Relapsed/Refractory multiple myeloma: A real-world experience. Transplant Cell Ther 30: 308.e13, 2024.
9. Tan CR, Asoori S, Huang CY, Brunaldi L, Popat R, Kastritis E, Martinez-Lopez J, Bansal R, Silva Corraes AM, Chhabra S, *et al*: Real-world evaluation of teclistamab for the treatment of relapsed/refractory multiple myeloma (RRMM): An International Myeloma Working Group study. Blood Cancer J 15: 53, 2025.
10. Charkviani M, Brochero MJV, Mohan A, Vaughan LE, Sandahl TB, De Menezes Silva Corrae A, Lin Y, Leung N and Herrmann SM: Incidence of acute kidney injury in relapsed and refractory multiple myeloma treated with teclistamab versus CAR T-cells. Nephrol Dial Transplant: gfaf004, 2025 doi: 10.1093/ndt/gfaf004 (Epub ahead of print).
11. Khouderchah CJ, Ochs M, Pianko M, Mahmoudjafari Z, Snyder J, Ahmed I, Campagnaro E and Nachar VR: Administration of teclistamab in four patients with multiple myeloma requiring hemodialysis. J Oncol Pharm Pract 30: 1089-1095, 2024.
12. Joiner L, Bal S, Godby KN and Costa LJ: Teclistamab in patients with multiple myeloma and impaired renal function. Am J Hematol 98: E322-E324, 2023.
13. Lebreton P, Lachenal F, Bouillie S, Pica GM, Aftisse H, Pascal L, Montes L, Macro M, Johnson N, Harel S, *et al*: Teclistamab for relapsed refractory multiple myeloma patients on dialysis. Br J Haematol 205: 2077-2079, 2024.
14. Riedhammer C, Bassermann F, Besemer B, Bewarder M, Brunner F, Carpinteiro A, Einsele H, Faltin J, Frenking J, Gezer D, *et al*: Real-world analysis of teclistamab in 123 RRMM patients from Germany. Leukemia 38: 365-371, 2024.