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Management of High-Risk Relapsed/Refractory Multiple Myeloma with Combination Chemo-Immunotherapy Leading to Allogeneic Stem Cell Transplantation

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BACKGROUND

Relapsed/refractory multiple myeloma (RRMM) featuring extramedullary involvement poses a therapeutic challenge with aggressive biology and poor prognosis. Standard chemotherapy regimens target proliferating plasma cells but frequently disrupt the bone marrow microenvironment, impairing endogenous immune surveillance. Bispecific antibodies targeting BCMA or GPRC5D redirect patient-derived cytotoxic T-cells toward myeloma cells, facilitating immune synapse formation and countering immunosuppressive signals. Selinexor complements these agents by promoting nuclear retention of tumor suppressors, inhibiting oncogenic protein export, and demonstrating synergistic effects with T-cell engagers.

PURPOSE

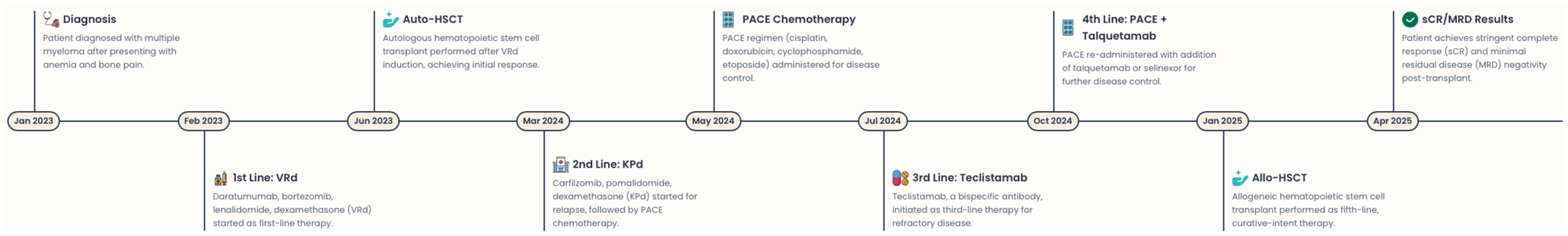
This case report demonstrates intensive multimodal therapy integrating bispecific antibodies, XPO1 inhibition, and multi-agent chemotherapy to salvage refractory extramedullary RRMM, enabling allogeneic hematopoietic stem cell transplantation (allo-HSCT) and potential long-term remission in a high-risk patient.

METHODS

A 42-year-old male was diagnosed in May 2022 with IgA-λ MM (R-ISS/stage II), high-risk due to complex karyotype, del(17p), and amp(1q). Initial treatment included six cycles daratumumab-VRd followed by melphalan 200mg/m² auto-HSCT (June 2023), yielding stringent complete response (sCR) maintained with daratumumab-lenalidomide. Biochemical relapse in March 2024 involved rising λ-free light chains, bone pain, and PET-CT-documented extramedullary lesions including biopsy-proven stomach and liver involvement. Second-line KPD plus cyclophosphamide-cisplatin-etoposide (two cycles, June-July 2024) produced partial response, but progression followed by late August 2024. One cycle of Teclistamab yielded no response, accompanied by additional extramedullary sites, liver-related ascites, and biopsy-proven retroorbital involvement. Salvage therapy comprised three cycles adriamycin-cisplatin-etoposide-cyclophosphamide-dexamethasone, then six cycles Talquetamab plus Selinexor.

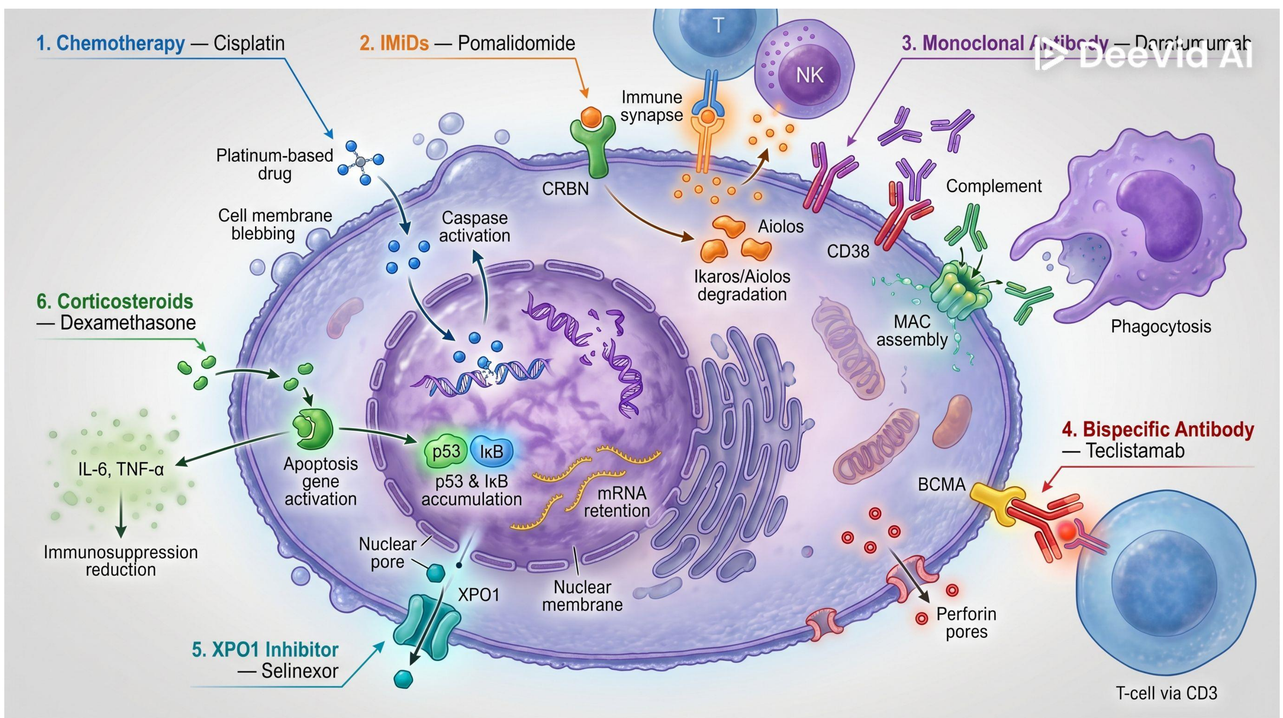
RESULTS

The regimen produced CR, permitting allo-HSCT from a matched unrelated donor in March 2025. Toxicity was manageable, no grade >3 AEs were noted. The patient achieved and maintains sCR with sustained MRD negativity at 10^{-6} by next-generation flow cytometry (EuroFlow) and PET-CT imaging.



CONCLUSIONS

Aggressive multimodal approaches effectively salvage refractory extramedullary RRMM, facilitating allo-HSCT and durable remission, supporting synergistic microenvironment modulation and T-cell redirection in umbrella trials.



Combined immuno-chemotherapy effect on Multiple Myeloma

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