



Original Article

Single Centre Experience of the Effect of Prior Administration of Daratumumab on Multiple Myeloma Patients Undergoing Autologous Stem Cell Transplantation

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ABSTRACT

Introduction: Multiple myeloma is a malignant disorder of terminally differentiated B lymphocytes characterized by uncontrolled clonal proliferation of plasma cells within the bone marrow microenvironment.

Aim: To evaluate the impact of prior daratumumab administration on stem cell mobilization, engraftment kinetics, infectious complications, and transplant outcomes in multiple myeloma patients undergoing autologous stem cell transplantation.

Methodology: This was a single-centre retrospective observational study conducted in the Department of medical oncology SMS Jaipur. **RESULT:** Prior administration of daratumumab was associated with adequate stem cell mobilization and satisfactory hematologic recovery, with mean neutrophil and platelet engraftment occurring at 11 and 14 days respectively. Although infectious complications were common (45%), transplant-related mortality remained low at 4%, indicating favorable short-term outcomes.

Conclusion: Daratumumab exposure prior to autologous stem cell transplantation does not appear to significantly compromise engraftment or overall survival, despite a modest delay in hematologic recovery. Infectious complications remain a notable concern; however, the procedure was generally well tolerated with high survival rates.

Keywords: Multiple myeloma, Daratumumab, stem cell transplantation.

INTRODUCTION

Multiple myeloma is a malignant disorder of terminally differentiated B lymphocytes characterized by uncontrolled clonal proliferation of plasma cells within the bone marrow microenvironment¹. This proliferation leads not only to classical end-organ damage—such as anemia, renal impairment, lytic bone lesions, and hypercalcemia—but also to profound immune dysfunction. A hallmark of the disease is suppression of normal immunoglobulin production, resulting in hypogammaglobulinemia and impaired humoral immunity.² Consequently, patients with multiple myeloma are intrinsically predisposed to infections even before the initiation of therapy. Over recent years, advances in therapeutic strategies—including proteasome inhibitors, immunomodulatory agents, and monoclonal antibodies—have significantly improved survival outcomes³. Among these agents, daratumumab, a human monoclonal antibody targeting CD38, has emerged as a key component of treatment in both newly diagnosed and relapsed or refractory multiple myeloma. Daratumumab exerts its antimyeloma effect through multiple immune-mediated mechanisms⁴. By binding to CD38 expressed on plasma cells, it induces complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity, antibody-dependent cellular phagocytosis, and direct apoptosis. These mechanisms contribute to deep and durable responses when daratumumab is incorporated into combination regimens. However, CD38 is not exclusively expressed on malignant plasma cells⁵. It is also present on various immune effector cells, including natural killer cells, subsets of T and B lymphocytes, and regulatory immune populations. As a result, daratumumab therapy may inadvertently alter normal immune homeostasis⁶. Depletion

or functional modulation of these immune cells can impair immune surveillance and antibody production, potentially exacerbating the pre-existing immunodeficiency associated with multiple myeloma. One clinically important consequence of this immunomodulatory effect is an increased susceptibility to infections. Respiratory tract infections, particularly upper respiratory infections and pneumonia, are among the most frequently observed non-hematologic adverse events in patients receiving daratumumab-containing regimens⁷. The mechanism underlying this increased risk is likely multifactorial, involving treatment-related neutropenia, suppression of normal immunoglobulin levels, and impaired cellular immunity. Furthermore, patients undergoing intensive therapies such as high-dose chemotherapy followed by autologous stem cell transplantation experience additional transient immunosuppression, which may further elevate infection risk during the early post-treatment period⁸. Despite recognition of infection as a potential adverse effect of daratumumab therapy, the precise magnitude and consistency of this risk remain incompletely defined. Variability in reported infection rates may reflect differences in disease stage, prior lines of therapy, treatment combinations, and definitions of infectious outcomes.⁹ Given the expanding role of daratumumab across multiple treatment settings, accurate quantification of infection risk is essential to optimize patient management. Preventive strategies—including vaccination against influenza, pneumococcus, and COVID-19, antiviral prophylaxis for herpes zoster during proteasome inhibitor or anti-CD38 therapy, selective antibacterial prophylaxis during high-risk periods, and intravenous immunoglobulin replacement in patients with recurrent infections and hypogammaglobulinemia—have become increasingly important components of supportive care.¹⁰

AIM

To evaluate the impact of prior daratumumab administration on stem cell mobilization, engraftment kinetics, infectious complications, and transplant outcomes in multiple myeloma patients undergoing autologous stem cell transplantation.

METHODOLOGY

This was a single-centre retrospective observational study conducted in the Department of medical oncology, SMS Jaipur. The study was carried out over a period of three years. All eligible patients were identified from hospital medical records and transplant databases. The study included adult patients (≥ 18 years) diagnosed with multiple myeloma who received daratumumab-containing induction therapy prior to undergoing autologous stem cell transplantation (ASCT). Only patients who completed stem cell mobilization and subsequently underwent ASCT during the study period were included. Clinical data including demographic details, CD34+ stem cell dose, time to neutrophil and platelet engraftment, infectious complications, transplant-related mortality, progression-free survival, and overall survival were collected and analyzed. Patients were excluded if they had undergone allogeneic stem cell transplantation, had incomplete medical records, did not receive daratumumab prior to transplant, or had active uncontrolled infection at the time of transplantation. Patients with concurrent malignancies or significant uncontrolled comorbid conditions were also excluded to minimize confounding factors. The study was conducted in accordance with institutional ethical standards, and patient confidentiality was maintained throughout the analysis.

RESULT

Table 1: Age Distribution of Patients

Age Group (Years)	Number of Patients (n)	Percentage (%)
18–30	4	16%
31–45	8	32%
46–60	9	36%
>60	4	16%

The majority of patients belonged to the 46–60 years age group (36%), followed by 31–45 years (32%). Patients aged 18–30 years and above 60 years each constituted 16% of the study population.

Table 2: Gender Distribution

Gender	Number (n)	Percentage (%)
Male	15	60%
Female	10	40%

Out of 25 patients, 15 (60%) were male and 10 (40%) were female. There was a male predominance with a male-to-female ratio of 1.5:1.

Table 3: CD34+ Stem Cell Dose Collected

CD34+ Cell Dose ($\times 10^6/\text{kg}$)	Number of Patients	Percentage (%)
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< 2 (Low)	6	24%
2 – 5	14	56%
> 5	5	20%

The majority of patients (56%) had a CD34+ stem cell dose between 2–5 ×10⁶/kg, while 20% achieved a dose greater than 5 ×10⁶/kg. A low CD34+ cell dose (<2 ×10⁶/kg) was observed in 24% of patients.

Table 4: Neutrophil and Platelet Engraftment

Parameter	Mean days	SD
Neutrophil Engraftment	11	2
Platelet Engraftment	14	3

The mean time to neutrophil engraftment was 11 ± 2 days, while platelet engraftment occurred at a mean of 14 ± 3 days. These findings indicate timely hematologic recovery following autologous stem cell transplantation.

Table 5: Infectious Complications Post-Transplant

Infection Type	Number (n)	Percentage (%)
Bacterial Infection	11	45%
Fungal Infection	4	16%
Pneumonia	8	32%
Septic Shock	1	5%

Infectious complications were observed in a significant proportion of patients, with bacterial infections occurring in 45% and fungal infections in 16% of cases. Pneumonia was reported in 32% of patients, while septic shock was noted in 5%, reflecting the burden of post-transplant infections.

Table 6: Transplant-Related Mortality

Outcome	Number (n)	Percentage (%)
Survived	24	96%
Mortality	1	4%

Out of 25 patients, 24 (96%) survived following autologous stem cell transplantation, while 1 patient (4%) experienced transplant-related mortality. The overall survival rate in the study cohort was therefore 96%.

DISCUSSION

In our study the age distribution of the study population demonstrated that the majority of patients belonged to the 46–60 years age group, accounting for 9 patients (36%). This was followed by the 31–45 years age group, which comprised 8 patients (32%). Patients aged 18–30 years constituted 4 cases (16%) of the total cohort. Similarly, 4 patients (16%) were above 60 years of age. The data indicate that most patients undergoing autologous stem cell transplantation were middle-aged adults.

Out of the total 25 patients included in our study, 15 were males and 10 were females.

Males constituted 60% of the study population, while females accounted for 40%. This indicates a male predominance among patients undergoing autologous stem cell transplantation. The male-to-female ratio in the present study was 1.5:1. Such gender distribution is consistent with the known epidemiology of multiple myeloma.

In our study The distribution of CD34+ stem cell dose showed that the majority of patients (56%) achieved a collection between 2–5 ×10⁶/kg. A total of 24% of patients had a low CD34+ cell dose of less than 2 ×10⁶/kg. Meanwhile, 20% of patients achieved a higher stem cell yield of more than 5 ×10⁶/kg. These findings indicate that although most patients attained an adequate stem cell collection, a significant proportion demonstrated suboptimal mobilization. The presence of low CD34+ yields reflect the impact of prior therapy on stem cell reserve. Nevertheless, successful stem cell collection was achieved in all patients who proceeded to transplantation. Eleutherakis Papaiakevou E et al¹¹ evaluated 200 newly diagnosed MM patients that were mobilized for SC collection and which received induction with (N = 40) or without daratumumab (N = 160). Dara group patients required more frequent use of plerixafor, larger collection volumes, and had

lower SC yield. 87.5% (35/40) of dara group patients achieved the planned yield of $\geq 5 \times 10^6$ CD34+/kg for at least one transplant compared to 96.2% (154/160) of patients in the non-dara group. Dara group patients had delayed hematopoietic recovery (11 vs 10 days for PMN $> 0.5 \times 10^9/l$), required more transfusions (4 vs 2 plts), prolonged hospitalization (20 vs 18 days), more febrile episodes and prolonged antibiotic administration. Despite the daratumumab effect, patients finally achieved a successful stem cell collection and proceeded to transplant. Our findings are similar to as reported by Eleutherakis Papaikovou et al¹¹, who observed lower stem cell yields and increased plerixafor use in patients receiving daratumumab-based induction compared to non-daratumumab regimens.

In our study the mean time to neutrophil engraftment was 11 days with a standard deviation of 2 days. This indicates that most patients achieved neutrophil recovery within a relatively narrow time range after transplantation. The mean time to platelet engraftment was 14 days with a standard deviation of 3 days. Platelet recovery occurred slightly later than neutrophil recovery, which is expected in the post-transplant period. The study suggests satisfactory hematologic recovery following autologous stem cell transplantation. Passucci M et al¹² Patients were divided in two groups: Arm A with 36 patients treated with D-VTD since January 2022, analysed prospectively; Arm B with 43 patients treated with VTD between 2020 and 2021 before daratumumab approval, analysed retrospectively. After a median follow-up of 21.2 months for the entire cohort (IQR 14.8 – 27.5), 62 patients have already received at least one ASCT (64% in Arm A vs 91% in arm B). After ASCT, median time of engraftment was significantly longer in arm A both for PMNs (11.0 vs 10.0 days, $p = 0.03$) and PLTs (15.0 vs 14.0 days, $p = 0.008$). Cavallaro et al¹³ reported a comparison between 109 TE-NDMM patients receiving induction therapy with D-VTD. Patients receiving D-VTD also showed a slower median time to neutrophils (PMNs) and platelets (PLTs) engraftment (13 vs 11 days in both cases, $p < 0.0001$); however, no differences were reported in terms of infection incidence between the two arms.

In our study Infectious complications were observed in a significant proportion of patients following transplantation. Bacterial infections were the most common, occurring in 11 patients (45%). Fungal infections were documented in 4 patients (16%), indicating additional opportunistic infectious risk. Pneumonia was reported in 8 patients (32%), representing a major respiratory complication. One patient (5%) developed septic shock, reflecting severe infection-related morbidity. These findings highlight the substantial burden of infectious complications in the early post-transplant period.

Out of the total 25 patients in our study who underwent autologous stem cell transplantation, 24 patients (96%) survived during the study period. Only one patient (4%) experienced mortality. The transplant-related mortality rate was therefore 4%. This indicates a high overall survival rate in the cohort. The low mortality suggests that the procedure was generally well tolerated. Despite the presence of infectious complications in some patients, the majority had favorable outcomes. Shimazu Y, et al¹⁴ performed a retrospective observational analysis. They analyzed 2626 patients who underwent ASCT between 2017 and 2020. In the comparison between patients not administered Dara (Dara- group) and those administered Dara (Dara+ group), the 1-year progression-free survival (PFS) rates were 87.4% and 77.3% and the 1-year overall survival (OS) rates were 96.7% and 90.0%, respectively.

CONCLUSION

In conclusion, our single-centre experience demonstrates that prior administration of daratumumab in multiple myeloma patients undergoing autologous stem cell transplantation is associated with acceptable stem cell mobilization and satisfactory hematologic recovery. Although a proportion of patients exhibited lower CD34+ stem cell yields, successful stem cell collection and transplantation were achieved in all eligible cases. Neutrophil and platelet engraftment occurred within expected timeframes, indicating adequate post-transplant marrow recovery. Infectious complications were observed in a considerable number of patients, with bacterial infections and pneumonia being the most frequent events; however, these were largely manageable with appropriate supportive care. The transplant-related mortality rate was low (4%), and overall survival during the study period was high (96%), reflecting favorable short-term outcomes. Overall, daratumumab administration prior to autologous stem cell transplantation appears to be feasible and clinically safe, with manageable infectious risks and satisfactory transplant outcomes in our cohort.

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