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MANAGEMENT OF PATIENTS WITH MULTIPLE MYELOMA FOLLOWING AUTOLOGOUS BONE MARROW TRANSPLANTATION

Nuriddin Najmiddinovich Temirov

Head of the Hematology Centre,

Samarkand Regional Multidisciplinary Medical Centre
Kadir Ergashevich Shomurodov

Hematologist, Hematology Centre,

Samarkand Regional Multidisciplinary Medical Centre
Dilafruz Abdikhalimovna Amerova

Assistant teachet of the Department of Hematology,

Samarkand State Medical University

Abstract. Autologous bone marrow transplantation (ABMT) remains a fundamental component of treatment for patients with multiple myeloma (MM), offering deep remission and prolonged survival when combined with modern therapeutic strategies. This study evaluates the clinical outcomes, complications, and effectiveness of post-transplant maintenance therapy in MM patients treated at a regional haematology centre in Uzbekistan. A total of 64 patients who underwent high-dose melphalan conditioning followed by ABMT were included. The majority achieved deep responses, with complete response (CR) in 62.5% and very good partial response (VGPR) in 21.9%. Lenalidomide-based maintenance therapy significantly improved 2-year progression-free survival (72% vs 45%, p = 0.038). Common post-transplant complications included infections (43.8%) and manageable non-infectious events such as mucositis and thrombocytopenia. No early transplant-related mortality occurred. These findings confirm the safety and efficacy of ABMT in MM and emphasise the importance of structured post-transplant management, including maintenance therapy and supportive care, to optimise long-term outcomes in resource-limited settings.

Keywords: Multiple myeloma, autologous transplantation, bone marrow transplant, maintenance therapy, lenalidomide, transplant complications, survival, Uzbekistan.

Introduction

Multiple myeloma (MM) is a clonal plasma cell malignancy that accounts for approximately 10–15% of haematologic cancers. It is characterised by uncontrolled proliferation of plasma cells in the bone marrow, leading to excessive monoclonal immunoglobulin production and subsequent organ damage, commonly referred to as the CRAB criteria (hyperCalcaemia, Renal insufficiency, Anaemia, and Bone lesions). Despite being considered incurable, the advent of novel therapies and the integration of autologous haematopoietic stem cell transplantation (AHSCT)—commonly known as autologous bone marrow transplantation (ABMT)—have significantly improved patient outcomes, transforming multiple myeloma into a chronic, manageable disease for many patients.

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Autologous transplantation has been the standard of care for transplant-eligible patients under 70 years of age with good performance status. It is typically performed after 3–6 cycles of induction chemotherapy using modern regimens containing bortezomib, lenalidomide, or thalidomide, followed by high-dose melphalan conditioning and reinfusion of the patient's previously collected stem cells. This approach allows for deep cytoreduction and achievement of minimal residual disease (MRD), which is now widely recognised as a major prognostic factor in long-term disease control.

The post-transplant period, however, represents a critical phase in the treatment trajectory. Despite successful stem cell engraftment and initial remission, patients are at considerable risk of relapse due to the persistence of residual malignant plasma cells. Without maintenance therapy, median progression-free survival (PFS) after ABMT is typically limited to 24–36 months. Hence, maintenance strategies—most commonly with lenalidomide—are routinely employed to extend remission, delay relapse, and potentially improve overall survival. However, maintenance therapy must be balanced with considerations of toxicity, financial burden, and patient-specific risk factors such as cytogenetics and comorbidities.

Another key challenge after ABMT is immune suppression. High-dose chemotherapy induces profound lymphopenia and delays immune reconstitution, predisposing patients to infections including bacterial pneumonias, herpes zoster reactivation, and fungal complications. In regions with limited access to prophylactic antimicrobial agents and supportive care, such infections can significantly impact survival and quality of life. Furthermore, prolonged use of steroids, bisphosphonates, and immunomodulatory drugs contributes to additional risks including osteonecrosis, gastrointestinal complications, cytopenias, and thromboembolic events.

In addition, comprehensive post-transplant management must address other long-term complications such as therapy-related myelodysplasia or secondary acute leukaemia, renal dysfunction progression, persistent bone disease, neuropathy, and psychological distress. These issues require an interdisciplinary and patient-centred approach, incorporating regular clinical monitoring, bone marrow assessments, imaging, laboratory surveillance, and appropriate psychosocial support.

Globally, the role of ABMT continues to evolve with the introduction of next-generation therapies such as CAR-T cells, bispecific antibodies, and monoclonal antibody-based induction regimens. Nevertheless, in resource-constrained settings like Uzbekistan, ABMT remains a highly valuable therapeutic intervention. In recent years, significant progress has been made in establishing transplant infrastructure and training specialists. However, structured post-transplant monitoring and data collection remain limited, which hinders evidence-based refinement of care pathways.

This study therefore aims to evaluate the outcomes, complications, and effectiveness of post-transplant management strategies in patients with multiple myeloma treated with autologous bone marrow transplantation at the Samarkand Regional Haematology Centre. By analysing clinical parameters, relapse rates, complications, infection profiles, and responses to maintenance therapies, this study will provide important insights into regional challenges and help inform national protocols. Ultimately, the findings may contribute to standardising

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post-ABMT care and improving survival and quality of life for patients living with multiple myeloma in Uzbekistan and similar healthcare environments.

Methodology

This retrospective observational study was conducted at the Haematology Centre of the Samarkand Regional Multidisciplinary Medical Centre between January 2019 and December 2023. The aim of the study was to assess the clinical outcomes, complications, and management strategies in patients with multiple myeloma (MM) following autologous bone marrow transplantation (ABMT). The study focused on evaluating relapse rates, post-transplant complications (particularly infections and cytopenias), effectiveness of maintenance therapy, and overall patient survival in a regional outpatient setting.

A total of 64 adult patients with a confirmed diagnosis of multiple myeloma who underwent ABMT during the study period were included. All patients met the International Myeloma Working Group (IMWG) criteria for symptomatic MM and were deemed eligible for high-dose therapy and autologous transplantation following initial induction chemotherapy. Patients with primary refractory disease, active infections at the time of transplant, or incomplete follow-up data were excluded from the analysis.

Transplant Protocol

All patients received high-dose melphalan (200 mg/m²) as a conditioning regimen prior to reinfusion of autologous haematopoietic stem cells, which had been harvested after induction therapy with bortezomib-based combinations (e.g., VCD – bortezomib, cyclophosphamide, dexamethasone or VRD – bortezomib, lenalidomide, dexamethasone). Stem cells were mobilised using granulocyte colony-stimulating factor (G-CSF) with or without cyclophosphamide. Supportive care included prophylactic antimicrobials, growth factors, and transfusion support according to institutional protocols.

Post-Transplant Monitoring and Management

Patients were followed for a minimum of 12 months post-transplant. Clinical assessments were conducted monthly for the first 6 months and every 2–3 months thereafter. Laboratory tests included complete blood counts, serum protein electrophoresis, serum free light chain assays, renal function tests, and inflammatory markers. Bone marrow biopsy and imaging (PET-CT or MRI) were performed as indicated to assess treatment response and disease progression. Response to treatment was assessed according to IMWG criteria, including complete response (CR), very good partial response (VGPR), partial response (PR), and progressive disease (PD). Minimal residual disease (MRD) evaluation was not routinely performed due to resource limitations. Patients who achieved at least VGPR post-transplant were offered maintenance therapy with lenalidomide (10 mg/day, 21 days per cycle), or thalidomide in resource-constrained cases. Those unable to tolerate maintenance due to toxicity were monitored off therapy.

Complications such as febrile neutropenia, herpes zoster reactivation, bacterial pneumonias, gastrointestinal toxicities, thromboembolic events, and cytopenias were recorded. Infection episodes were classified according to severity and need for hospitalisation. Supportive therapies—including bisphosphonates, erythropoietin, and prophylactic antivirals or antifungals—were documented.

Statistical Analysis

All collected data were anonymised and entered into a central database. Statistical analysis was performed using SPSS version 26.0. Descriptive statistics were used to summarise demographic and clinical data. Kaplan–Meier curves were generated to estimate progression-free survival (PFS) and overall survival (OS). Differences in outcomes between

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subgroups (e.g., maintenance vs no maintenance) were assessed using the log-rank test. A p-value < 0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Ethics Committee of Samarkand State Medical University. Informed consent for treatment and data use was obtained from all patients prior to transplantation.

Results

A total of 64 patients with multiple myeloma (MM) who underwent autologous bone marrow transplantation (ABMT) at the Samarkand Regional Haematology Centre were included in the analysis. The median age was 58 years (range: 42–70), with a male-to-female ratio of 1.2:1. Most patients (87.5%) had IgG-type myeloma, while the remaining had IgA or light chain-only variants. High-risk cytogenetic abnormalities (such as del(17p) or t(4;14)) were present in 14.1% of patients, based on fluorescence in situ hybridisation (FISH) testing where available.

Transplant Outcomes

All patients underwent high-dose melphalan conditioning and stem cell reinfusion. Neutrophil engraftment was achieved at a median of day +11 (range: 9–15), and platelet engraftment occurred by day +14 (range: 11–21). Early transplant-related mortality was 0%, indicating a high safety profile of the ABMT procedure in this setting. Following transplantation, 90.6% of patients (58 out of 64) achieved at least a partial response (PR), with 62.5% achieving complete response (CR) and 21.9% achieving very good partial response (VGPR). Six patients (9.4%) had only a minimal response or stable disease. Response depth was strongly correlated with the quality of the pre-transplant induction response ($p < 0.01$). MRD assessment was not performed routinely due to resource constraints.

Maintenance Therapy and Relapse Rates

Out of 58 patients who achieved VGPR or better, 40 (69%) received lenalidomide-based maintenance therapy, while 6 received thalidomide due to drug availability. The remaining 12 patients (20.6%) declined or could not tolerate maintenance therapy due to adverse effects such as cytopenia, fatigue, or thromboembolic complications.

After a median follow-up of 22 months (range: 12–46 months), 13 patients (20.3%) experienced disease progression. The 2-year progression-free survival (PFS) rate was 72% in the maintenance group versus 45% in those without maintenance ($p = 0.038$). The overall survival (OS) rate at 2 years was 85%, with only 6 recorded deaths—3 due to disease progression and 3 due to infectious complications during relapse treatment.

Post-Transplant Complications

Infectious complications were reported in 28 patients (43.8%). The most common were bacterial infections (particularly pneumonia and urinary tract infections), followed by herpes zoster reactivation (7 cases) and one case of probable invasive aspergillosis. Most infections were managed with outpatient antimicrobial therapy, but 9 patients required hospitalisation. No deaths were attributed to early infectious complications.

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Non-infectious complications included:

- Grade II–III thrombocytopenia lasting beyond day +30 in 18.7% of patients
- Peripheral neuropathy (mostly due to thalidomide) in 5 patients
- One case of venous thromboembolism (VTE) despite prophylaxis
- Gastrointestinal toxicity (nausea, diarrhoea, mucositis) in 32.8% of patients, all self-limiting

Bone disease was monitored in all patients. Monthly bisphosphonate therapy (zoledronic acid) was administered to 87.5% of the cohort. No new skeletal-related events were reported during the follow-up period.

Statistical Findings

Patients who achieved CR post-transplant and received lenalidomide maintenance had significantly longer PFS compared to those with PR or no maintenance ($p < 0.05$). High-risk cytogenetics were associated with shorter time to relapse, although this did not reach statistical significance ($p = 0.08$), likely due to the limited number of high-risk patients in the sample.

In summary, ABMT was safe and effective for multiple myeloma patients in this regional setting, with high response rates and low transplant-related mortality. Maintenance therapy with lenalidomide significantly prolonged PFS. Infectious complications were frequent but mostly manageable. These findings highlight the importance of structured post-transplant care, including maintenance, infection monitoring, and bone support, to improve outcomes in real-world clinical practice.

Discussion

The findings of this study confirm the clinical efficacy and safety of autologous bone marrow transplantation (ABMT) in patients with multiple myeloma (MM), reflecting outcomes comparable to international benchmarks despite the resource-constrained setting. High overall response rates, low transplant-related mortality, and acceptable complication profiles demonstrate the viability of ABMT as a standard consolidation therapy for transplant-eligible MM patients in Uzbekistan.

A key outcome of this study is the post-transplant response profile, with 62.5% of patients achieving complete response (CR) and an additional 21.9% reaching very good partial response (VGPR). These rates are consistent with major studies such as IFM 2009 and CALGB 100104, which support the use of high-dose melphalan followed by ABMT to achieve deep, durable remissions. Moreover, the absence of early transplant-related deaths, alongside timely engraftment, suggests that current transplantation protocols are both clinically sound and well-tolerated by the local patient population.

Another significant observation is the impact of post-transplant maintenance therapy on disease control. Patients who received lenalidomide maintenance showed a substantially higher 2-year progression-free survival (PFS) compared to those who did not (72% vs 45%, $p = 0.038$), confirming findings from large trials such as the Myeloma XI and IFM 2005-02

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studies. Although maintenance therapy is associated with certain side effects, its benefits in prolonging remission and delaying relapse clearly outweigh its risks when appropriately monitored. Thalidomide, though used in a limited number of patients due to resource limitations, remains a viable alternative in low-income settings despite its inferior side effect profile.

The incidence of infections (43.8%) post-transplant, including herpes zoster reactivation and bacterial pneumonias, highlights the need for continued infection prophylaxis and early detection strategies. While most infections were manageable on an outpatient basis, approximately 14% required hospitalisation. This reinforces the importance of structured outpatient follow-up, vaccination protocols, and rapid response systems to mitigate infection-related morbidity in immunocompromised patients.

Non-infectious complications such as persistent thrombocytopenia, mucositis, and neuropathy were observed but largely manageable. Notably, long-term bone support with bisphosphonates prevented further skeletal-related events, underscoring the importance of comprehensive supportive care in the post-transplant setting.

The relatively low relapse rate observed (20.3%) during the median follow-up period is promising. However, the presence of high-risk cytogenetics in a subset of patients correlated with shorter PFS, suggesting a need for future incorporation of risk-adapted strategies, such as tandem transplantation or early integration of novel agents like monoclonal antibodies or CAR-T cells. Although MRD monitoring was not feasible in this cohort, its adoption could significantly enhance response evaluation and guide post-transplant interventions.

Importantly, the findings of this study have practical implications for clinical practice in Uzbekistan and similar healthcare systems. With increasing access to transplantation services, there is a pressing need to develop standardised post-ABMT care protocols that include maintenance therapy, infection prophylaxis, psychosocial support, and timely laboratory and imaging surveillance. Investment in diagnostic infrastructure, particularly for MRD assessment and cytogenetic profiling, would further enable precision-guided management.

In conclusion, ABMT remains a cornerstone in the treatment of multiple myeloma in transplant-eligible patients. When coupled with effective post-transplant maintenance and supportive care, it offers durable disease control and improved survival. This study provides strong regional evidence supporting the continued use and refinement of ABMT in Uzbekistan and offers a foundation for further prospective, multicentre research to optimise MM management.

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