Multiple Myeloma

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KEYWORDS

- Immunomodulatory agents • Proteasome inhibitors • Maintenance therapy
- Reduced-intensity conditioning

KEY POINTS

- Patients eligible for high-dose therapy typically undergo induction therapy followed by upfront autologous stem cell transplant. Whether transplant can be delayed until time of first relapse with equivalent long-term outcomes is currently under study.
- Single-agent high-dose melphalan remains the standard of care for the high-dose regimen for autologous stem cell transplant.
- Reduced-intensity conditioning regimens for allogeneic transplant have improved transplant-related mortality rates, but disease relapse, graft-versus-host disease, and treatment-related mortality remain significant problems.
- Salvage autologous stem cell transplant is feasible and seems to be most effective for patients who have relapse at least 18 months or later from their initial transplant.
- The therapeutic landscape for myeloma is evolving rapidly, impacting both pre- and post-transplant treatment strategies.

INTRODUCTION

Induction therapy followed by consolidation with high-dose melphalan and autologous stem cell transplant (ASCT) has been considered the standard of care for transplant-eligible myeloma patients for several decades. The role of allogeneic stem cell transplant (AlloSCT) has been less clear, as both myeloablative and reduced-intensity approaches have been fraught with transplant-related mortality, graft versus host disease (GvHD), and disease relapse. In today's era of novel agents, which include the immunomodulatory agents (thalidomide, lenalidomide, pomalidomide) and proteasome inhibitors (bortezomib and carfilzomib), several unanswered questions remain regarding the role of transplant. These unresolved issues include the timing of initial transplant (upfront after induction therapy vs delayed until time of first relapse or later), the incorporation of novel agents into the high-dose regimen, the optimal maintenance regimen after transplant, the role of novel agents versus salvage (second) transplant after relapse from the first transplant, and the role of AlloSCT. In this article we provide an overview of transplantation for myeloma and discuss the areas that remain under active investigation.

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PATIENT EVALUATION OVERVIEW

As denoted in Table 1, the standard pretransplant evaluation includes assessment of organ function, infectious disease status, psychosocial status, and myeloma restaging. Human leukocyte antigen (HLA) typing is performed for patients being considered for AlloSCT and possibly for younger patients being considered for autologous stem cell transplant who could potentially be offered AlloSCT in the future.

INDICATIONS FOR TRANSPLANT

Traditionally, all patients younger than 65 years with adequate organ function and performance status and who have achieved disease control have been considered candidates for ASCT. Most transplant centers in the United States, however, will perform transplants on patients up to the age 75, and some centers have no age limit but instead rely on performance status and adequate organ function. Multiple studies have shown the feasibility and efficacy of performing ASCT in elderly patients.[1–5] The role of AlloSCT in myeloma continues to be debated.[6] Outside of a clinical trial, it is most often considered for younger patients with high-risk disease in either the upfront setting or after an early relapse after ASCT (Box 1, Fig. 1).

Table 1
Pretransplant evaluation

Test	Notes
Renal function	Creatinine clearance <50 mL/min may result in a dose modification of the high-dose melphalan
Hepatic function	Direct bilirubin, alkaline phosphatase, AST/ALT <3× normal
Myeloma restaging	Quantitative immunoglobulins, serum immunofixation electrophoresis (IFE), serum protein electrophoresis, urine IFE, urine protein electrophoresis, serum free light chains, skeletal survey, bone marrow aspirate/biopsy with standard karyotyping and FISH panel of CD138-selected cells, flow cytometry
PET/CT scan	Considered for patients with plasmacytoma
Pulmonary function tests	DLCO or DLVA ≥50% predicted; DLCO to be corrected for hemoglobin and/or alveolar ventilation
Cardiac function: ECG and echocardiogram/MUGA	Left ventricular ejection fraction (LVEF) ≥50% or cardiology consult if LVEF <50%
Osteoporosis evaluation	DEXA, vitamin D
Infectious disease testing	CMV immunoglobulin G/immunoglobulin M, hepatitis B/C, HIV, HTLV, Treponemal pallidum
HLA typing	If AlloSCT to be considered
Psychosocial evaluation	Social work evaluation, patient and caregiver orientation, family meeting
Dental consult	To evaluate for osteonecrosis of the jaw or severe dental problems that could complicate bisphosphonate use
Physical therapy consult	Maintaining strength after transplant
Dietary consult	Consideration for nutritional supplementation such as total parenteral nutrition following transplant

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; CMV, cytomegalovirus; DEXA, dual-energy x-ray absorptiometry; DLCO, diffusing capacity of carbon monoxide; DLVA, DLCO adjusted for volume; ECG, electrocardiogram; FISH, fluorescence in situ hybridization; HIV, human immunodeficiency virus; HTLV, human T-lymphotropic virus; IFE, immunofixation electrophoresis; LVEF, left ventricular ejection fraction; MUGA, multigated acquisition; PET, positron emission tomography.

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