Medical Policy

Hematopoietic Stem Cell Transplantation for Plasma Cell Dyscracias, Including Multiple Myeloma and POEMS Syndrome

Table of Contents

Policy Number: 075

BCBSA Reference Number: 8.01.17

Related Policies

None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

Multiple myeloma

A single or second (salvage) autologous hematopoietic stem-cell transplantation may be **MEDICALLY NECESSARY** to treat multiple myeloma.

Tandem autologous-autologous hematopoietic stem-cell transplantation may be **MEDICALLY NECESSARY** to treat multiple myeloma in patients who fail to achieve at least a near-complete or very good partial response after the first transplant in the tandem sequence.

Definition of near-complete response and very good partial response

- A near complete response, as defined by the European Group for Blood and Marrow Transplant (EBMT) is the disappearance of M protein at routine electrophoresis, but positive immunofixation.
- A very good partial response has been defined as a 90% decrease in the serum paraprotein level.

Tandem transplantation with an initial round of autologous hematopoietic stem-cell transplantation followed by a non-marrow-ablative conditioning regimen and allogeneic hematopoietic stem-cell transplantation (i.e., reduced-intensity conditioning transplant) may be **MEDICALLY NECESSARY** to treat newly diagnosed multiple myeloma patients.

Allogeneic hematopoietic stem-cell transplantation, myeloablative or nonmyeloablative, as upfront therapy of newly diagnosed multiple myeloma or as salvage therapy, is **INVESTIGATIONAL**.

POEMS syndrome
Autologous hematopoietic stem-cell transplantation may be considered **MEDICALLY NECESSARY** to treat disseminated POEMS syndrome.

Allogeneic and tandem hematopoietic stem-cell transplantation are **INVESTIGATIONAL** to treat POEMS syndrome.

Prior Authorization Information

Commercial Members: Managed Care (HMO and POS)
Prior authorization is required.

Commercial Members: PPO, and Indemnity
Prior authorization is required.

Medicare Members: HMO Blue[SM]
Prior authorization is required.

Medicare Members: PPO Blue[SM]
Prior authorization is required.

CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member. A draft of future ICD-10 Coding related to this document, as it might look today, is included below for your reference.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

CPT codes:	Code Description
38204	Management of recipient hematopoietic cell donor search and cell acquisition
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion with harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor-cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
38220	Bone marrow; aspiration only
38221	Bone marrow; biopsy, needle or trocar
38230	Bone marrow harvesting for transplantation; allogeneic

38232	Bone marrow harvesting for transplantation; autologous
38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic
38241	Bone marrow or blood-derived peripheral stem-cell transplantation; autologous

HCPCS Codes

HCPCS codes:	Code Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived peripheral stem-cell (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications including pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre- and post-transplant care in the global definition

ICD-9 Diagnosis Codes

ICD-9-CM diagnosis codes:	Code Description
203.00	Multiple myeloma, without mention of having achieved remission
203.01	Multiple myeloma, in remission
203.02	Multiple myeloma, in relapse

ICD-9 Procedure Codes

ICD-9-CM procedure codes:	Code Description
41.00	Bone marrow transplant, not otherwise specified
41.01	Autologous bone marrow transplant without purging
41.02	Allogeneic bone marrow transplant with purging
41.03	Allogeneic bone marrow transplant without purging
41.04	Autologous hematopoietic stem cell transplant without purging
41.05	Allogeneic hematopoietic stem cell transplant without purging
41.06	Cord blood stem cell transplant
41.07	Autologous hematopoietic stem cell transplant with purging
41.08	Allogeneic hematopoietic stem cell transplant with purging
41.09	Autologous bone marrow transplant with purging

ICD-10-CM Diagnosis Codes

ICD-10-CM diagnosis codes:	Code Description
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma in relapse

ICD-10-PCS Procedure Codes

ICD-10-PCS procedure	Code Description

codes:	
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30233Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30263Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
30233X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30243X0	Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30263X0	Transfusion of Autologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach
30263X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach

30263Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach
30233Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30263Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

Description

Hematopoietic Stem-Cell Transplantation

Hematopoietic stem-cell transplantation (HSCT) refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without whole-body radiation therapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD.

Background

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HSCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HSCT. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the Class I and Class II loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (with the exception of umbilical cord blood).

Conventional Preparative Conditioning for HSCT

The conventional (“classical”) practice of allogeneic HSCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total-body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect mediated by non-self immunologic effector cells that develop after engraftment of allogeneic stem cells within the patient’s bone marrow space. While the slower GVM effect is considered to be the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit

medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HSCT, immunosuppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections.

The success of autologous HSCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allogeneic HSCT
Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less-intense regimens of cytotoxic drugs or radiation than are used in traditional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and non-relapse mortality (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic HSCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells.

For the purposes of this Policy, the term "reduced-intensity conditioning" will refer to all conditioning regimens intended to be non-myeloablative, as opposed to fully myeloablative (traditional) regimens.

Multiple Myeloma
Multiple myeloma (MM) is a systemic malignancy of plasma cells that represents approximately 10% of all hematologic cancers. It is treatable but rarely curable. At the time of diagnosis, most patients have generalized disease, and, the selection of treatment is influenced by patient age, general health, prior therapy, and the presence of complications of the disease. (1, 2)
The disease is staged by estimating tumor mass, based on various clinical parameters such as hemoglobin, serum calcium, number of lytic bone lesions, and the presence or absence of renal failure. Multiple myeloma usually evolves from an asymptomatic premalignant stage (termed "monoclonal gammopathy of undetermined significance" or MGUS). Treatment is usually reserved for patients with symptomatic disease (usually progressive myeloma), whereas asymptomatic patients are observed, as there is little evidence that early treatment of asymptomatic multiple myeloma prolongs survival when compared to therapy delivered at the time of symptoms or end-organ damage.(1, 2) In some patients, an intermediate asymptomatic but more advanced premalignant stage is recognized and referred to as smoldering multiple myeloma. The overall risk of disease progression from smoldering to symptomatic multiple myeloma is 10% per year for the first 5 years, approximately 3% per year for the next 5 years, and 1% for the next 10 years.(1, 2)

POEMS Syndrome
POEMS syndrome (also known as osteosclerotic myeloma, Crow-Fukase syndrome, or Takasuki syndrome) is a rare, paraneoplastic disorder secondary to a plasma-cell dyscrasia. (3, 4) This complex, multiorgan disease was first described in 1938, but the acronym POEMS was coined in 1980, reflecting hallmark characteristics of the syndrome: polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. (5) No single test establishes the presence of POEMS syndrome. Its pathogenesis is

undefined, although some evidence suggests it is mediated by imbalance of proinflammatory cytokines including interleukin-1β (IL-1β), IL-6, and tumor necrosis factor-α; vascular endothelial growth factor may also be involved. (4, 6) However, specific criteria have been established, and the syndrome may entail other findings in the constellation of signs and symptoms, as shown in the Table. Both major criteria and at least one of the minor criteria are necessary for diagnosis. (6)

Criteria for the diagnosis of POEMS syndrome (4**,** 6**)**

Major Criteria	**Minor Criteria**	**Known Associations**	**Possible Associations**
Polyneuropathy	Sclerotic bone lesions	Clubbing	Pulmonary hypertension
Monoclonal plasmaproliferative disorder	Castleman disease	Weight loss	Restrictive lung disease
	Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy)	Thrombocytosis	Thrombotic diatheses
		Polycythemia	Arthralgias
	Edema (edema, pleural effusion, or ascites)	Hyperhidrosis	Cardiomyopathy (systolic dysfunction)
	Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic)		Fever
	Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails)		Low vitamin B12 values
			Diarrhea
	Papilledema		

The prevalence of POEMS syndrome is unclear. A national survey in Japan showed a prevalence of about 0.3 per 100,000.(7) Other large series have been described in the United States (4, 6, 8) and in India.(9) In general, patients with POEMS have a superior overall survival compared with that of MM, nearly 14 years in a large series from the Mayo Clinic. (6) However, given the rarity of POEMS, no randomized controlled trials of therapies have been reported. (10) Numerous approaches have included ionizing radiation, plasmapheresis, intravenous immunoglobulin, interferon alfa, corticosteroids, alkylating

agents, azathioprine, tamoxifen, transretinoic acid, and high-dose chemotherapy with autologous HSCT support. (4, 6) Optimal treatment involves eliminating the plasma cell clone, for example, by surgical excision or local radiation therapy for an isolated plasmacytoma, or systemic chemotherapy in patients with disseminated disease, such as medullary disease or multiple plasmacytomas. Given the underlying plasma cell dyscrasia of POEMS, newer approaches to MM, including bortezomib, lenalidomide, and thalidomide, are also under investigation. (4, 11)

Summary

No RCTs of hematopoietic stem-cell transplantation (HSCT) have been performed in patients with POEMS syndrome, nor is it likely such studies will ever be performed given the rarity of this condition. Available case reports and series are subject to selection bias and are heterogeneous with respect to treatment approaches and peri-transplant support. However, for autologous HSCT, a chain of indirect evidence suggests improved health outcomes, as several case studies have reported good clinical responses. In addition, certain contextual factors and strong clinical consensus support that autologous HSCT may be considered medically necessary for disseminated POEMS syndrome. Allogeneic and tandem HSCT are considered investigational to treat POEMS syndrome.

Policy History

Date	Action
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
2/2014	BCBSA National medical policy review. New medically necessary and investigational indications described; policy title changed. Effective 2/1/2014.
12/2012	Updated to add new CPT code 38243
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/2011	Minor change to policy statements (added phrase “in the tandem sequence” to the medically necessary tandem autologous-autologous statement).
7/2011	Medical Policy Group – Hematology and Oncology. No changes to policy statements.
9/2010	Medical Policy Group – Hematology and Oncology. No changes to policy statements.
9/1/2010	Medical Policy 075 effective 9/1/2010.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

1. Kyle RA, Rajkumar SV. Multiple myeloma. Blood 2008; 111(6):2962-72.
2. Palumbo A, Rajkumar SV. Treatment of newly diagnosed myeloma. Leukemia 2009; 23(3):449-56.
3. Dispenzieri A. Long-term outcomes after autologous stem cell transplantation in patients with POEMS syndrome. Clin Adv Hematol Oncol 2012; 10(11):744-6.
4. Dispenzieri A. POEMS syndrome: update on diagnosis, risk-stratification, and management. Am J Hematol 2012; 87(8):804-14.
5. Bardwick PA, Zvaifler NJ, Gill GN et al. Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes: the POEMS syndrome. Report on two cases and a review of the literature. Medicine (Baltimore) 1980; 59(4):311-22.

6. Dispenzieri A, Kyle RA, Lacy MQ et al. POEMS syndrome: definitions and long-term outcome. Blood 2003; 101(7):2496-506.
7. Nasu S, Misawa S, Sekiguchi Y et al. Different neurological and physiological profiles in POEMS syndrome and chronic inflammatory demyelinating polyneuropathy. J Neurol Neurosurg Psychiatry 2012; 83(5):476-9.
8. Dispenzieri A, Moreno-Aspitia A, Suarez GA et al. Peripheral blood stem cell transplantation in 16 patients with POEMS syndrome, and a review of the literature. Blood 2004; 104(10):3400-7.
9. Singh D, Wadhwa J, Kumar L et al. POEMS syndrome: experience with fourteen cases. Leuk Lymphoma 2003; 44(10):1749-52.
10. Kuwabara S, Dispenzieri A, Arimura K et al. Treatment for POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome. Cochrane Database Syst Rev 2012; 6:CD006828.
11. Dispenzieri A. How I treat POEMS syndrome. Blood 2012; 119(24):5650-8.
12. Blade J, Samson D, Reece D, et al. Criteria for evaluating disease response and progression in patients with multiple myeloma treated by high-dose therapy and haemopoietic stem cell transplantation. Myeloma Subcommittee of the EBMT. Br J Haematol 1998; 102(5):1115-23.
13. Fermand JP, Katsahian S, Divine M et al. High-dose therapy and autologous blood stem-cell transplantation compared with conventional treatment in myeloma patients aged 55 to 65 years: long-term results of a randomized control trial from the Group Myelome-Autogreffe. J Clin Oncol 2005; 23(36):9227-33.
14. Reece DE. Recent trends in the management of newly diagnosed multiple myeloma. Curr Opin Hematol 2009; 16(4):306-12.
15. Reece D, Harousseau JL, Gertz MA. Myeloma Management 2009: Nontransplant therapy of myeloma, high-dose therapy for myeloma, and apersonalized care plan for treatment of myeloma. 2009 American Society of Clinical Oncology Annual Meeting Educational Handbook/ 2009:502-9.
16. Fonseca R. Strategies for risk-adapted therapy in myeloma. Hematology Am Soc Hematol Educ Program 2007:304-10.
17. Rajkumar SV. Multiple myeloma: 2011 update on diagnosis, risk-stratification, and management. Am J Hematol 2011; 86(1):57-65.
18. Larocca A, Palumbo A. Evolving paradigms in the treatment of newly diagnosed multiple myeloma. J Natl Compr Canc Netw 2011; 9(10):1186-96.
19. van de Donk NW, Lokhorst HM, Dimopoulos M et al. Treatment of relapsed and refractory multiple myeloma in the era of novel agents. Cancer Treat Rev 2011; 37(4):266-83.
20. Nishihori T, Alsina M. Advances in the autologous and allogeneic transplantation strategies for multiple myeloma. Cancer Control 2011; 18(4):258-67.
21. Attal M, Harousseau JL. The role of high-dose therapy with autologous stem cell support in the era of novel agents. Semin Hematol 2009; 46(2):127-32.
22. Attal M, Harousseau JL, Stoppa AM et al. A prospective randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. N Engl J Med 1996; 335(2):91-7.
23. Barlogie B, Kyle RA, Anderson KC et al. Standard chemotherapy compared with high-dose chemoradiotherapy for multiple myeloma: final results of phase III US Intergroup Trial 9321. J Clin Oncol 2006; 24(6):929-36.
24. Blade J, Rosinol L, Sureda A et al. High-dose therapy intensification compared with continued standard chemotherapy in multiple myeloma patients responding to the initial chemotherapy: long-term results from a prospective randomized trial from the Spanish Cooperative Group PETHEMA. Blood 2005; 106(12):3755-9.
25. Child JA, Morgan GJ, Davies FE et al. High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. N Engl J Med 2003; 348(19):1875-83.
26. Fermand JP, Ravaud P, Chevret S et al. High-dose therapy and autologous peripheral blood stem-cell transplantation in multiple myeloma: upfront or rescue treatment? Results of a multicenter sequential randomized trial. Blood 1998; 92(9):3131-6.
27. Palumbo A, Bringhen S, Petrucci MT et al. Intermediate-dose melphalan improves survival of myeloma patients aged 50-70: results of a randomized controlled trial. Blood 2004; 104(10):3052-7.

28. Koreth J, Cutler CS, Djulbegovic B et al. High-dose therapy with single autologous transplantation versus chemotherapy for newly diagnosed multiple myeloma: a systematic review and meta-analysis of randomized controlled trials. Biol Blood Marrow Transplant 2007; 13(2):183-96.
29. Bensinger WI. Role of autologous and allogeneic stem cell transplantation in myeloma. Leukemia 2009; 23(3):442-8.
30. Olin RL, Vogl DT, Porter DL et al. Second auto-SCT is safe and effective salvage therapy for relapsed multiple myeloma. Bone Marrow Transplant 2009; 43(5):417-22.
31. Hahn T, Wingard JR, Anderson KC et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of multiple myeloma: an evidence-based review. Biol Blood Marrow Transplant 2003; 9(1):4-37.
32. Qazilbash MH, Saliba R, De Lima M et al. Second autologous or allogeneic transplantation after the failure of first autograft in patients with multiple myeloma. Cancer 2006; 106(5):1084-9.
33. Attal M, Harousseau JL, Facon T et al. Single versus double autologous stem-cell transplantation for multiple myeloma. N Engl J Med 2003; 349(26):2495-502.
34. Stadtmauer EA. Multiple myeloma, 2004--one or two transplants? N Engl J Med 2003; 349(26):2551-3.
35. Cavo M, Tosi P, Zamagni E et al. Prospective, randomized study of single compared with double autologous stem-cell transplantation for multiple myeloma: Bologna 96 clinical study. J Clin Oncol 2007; 25(17):2434-41.
36. Garban F, Attal M, Michallet M et al. Prospective comparison of autologous stem cell transplantation followed by dose-reduced allograft (IFM99-03 trial) with tandem autologous stem cell transplantation (IFM99-04) trial in high-risk de novo multiple myeloma. Blood 2006; 107(9):3474-80.
37. Moreau P, Garban F, Attal M et al. Long-term follow-up results of IFM99-03 and IFM99-04 trials comparing nonmyeloablative allotransplantation with autologous transplantation in high-risk de novo multiple myeloma. Blood 2008; 112(9):3914-5.
38. Bruno B, Rotta M, Patriarca F et al. A comparison of allografting with autografting for newly diagnosed myeloma. N Engl J Med 2007; 356(11):1110-20.
39. Rosinol L, Perez-Simon JA, Sureda A et al. A prospective PETHEMA study of tandem autologous transplantation versus autograft followed by reduced-intensity conditioning allogeneic transplantation in newly diagnosed multiple myeloma. Blood 2008; 112(9):3591-3.
40. Lokhorst H, Mutis, I. Allogeneic transplantation and immune interventions in multiple myeloma. Hematology Education: the education program for the annual congress of the European Hematology Association, 2008; 2:106-14.
41. Bjorkstrand B, Iacobelli S, Hegenbart U et al. Autologous stem cell transplantation (ASCT) versus ASCT followed by reduced-intensity conditioning allogeneic SCT with identical sibling donor in previously untreated multiple myeloma: preliminary analysis of a prospective controlled trial by the EBMT. Bone Marrow Transplant 2008; 41:S38.
42. Gahrton G, Bjorkstrand B. Allogeneic transplantation in multiple myeloma. Haematologica 2008; 93(9):1295-300.
43. Krishnan A, Pasquini MC, Logan B et al. Autologous haemopoietic stem-cell transplantation followed by allogeneic or autologous haemopoietic stem-cell transplantation in patients with multiple myeloma (BMT CTN 0102): a phase 3 biological assignment trial. Lancet Oncol 2011; 12(13):1195-203.
44. Harousseau JL. The allogeneic dilemma. Bone Marrow Transplant 2007; 40(12):1123-8.
45. Crawley C, Iacobelli S, Bjorkstrand B et al. Reduced-intensity conditioning for myeloma: lower nonrelapse mortality but higher relapse rates compared with myeloablative conditioning. Blood 2007; 109(8):3588-94.
46. Lokhorst H, Einsele H, Vesole D et al. International Myeloma Working Group consensus statement regarding the current status of allogeneic stem-cell transplantation for multiple myeloma. J Clin Oncol 2010; 28(29):4521-30.
47. D'Souza A, Lacy M, Gertz M et al. Long-term outcomes after autologous stem cell transplantation for patients with POEMS syndrome (osteosclerotic myeloma): a single-center experience. Blood 2012; 120(1):56-62.