

# Autologous stem cell transplantation in multiple myeloma

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## Introduction

Myeloma is the malignant proliferation of plasma cells. It is the second most common haematological malignancy after non-Hodgkin's lymphoma, comprising 10% of all haematological malignancies and 1% of all cancers. There is a slight predominance in males and blacks. The aetiology is still uncertain, but an increased risk of myeloma has been noted in survivors of the Hiroshima and Nagasaki disasters, radiation workers and sheet metal workers. There is a direct relationship with increasing age and it is very rarely seen in patients below the age of 40.

## Clinical presentation of multiple myeloma

Multiple myeloma is characterised by the excessive production of monoclonal proteins and a reduction in the number of normal plasma cells, leading to a decrease in immunoglobulin production and an increase in the risk of infections, especially of the urinary tract and the respiratory system. Infiltration of the bone marrow by these malignant plasma cells leads to bone marrow failure, manifesting as anaemia and other cytopenias. The excessive secretion of monoclonal immunoglobulins by the malignant cells can cause hyperviscosity, and deposition of immunoglobulin light chains can give rise to amyloidosis. Patients frequently develop renal failure and bone complications with lytic lesions being formed in the axial skeleton. This leads to weakening of the bone with an increased risk of pathological fractures and excessive bone resorption, which manifests clinically as hypercalcaemia.

## Treatment of multiple myeloma

Autologous stem cell transplantation (SCT) following high-dose myeloablative chemotherapy has become the standard of care for patients younger than 65 years of age with newly diagnosed multiple myeloma. While myeloma still remains an incurable disease, both overall and event-free survival are prolonged following autologous SCT when compared with conventional chemotherapy.

A successful outcome after autologous SCT is based on the presumption that residual myeloma cells will be destroyed by the high-dose chemotherapy that is administered before stem cell reinfusion. Unfortunately, healthy bone marrow progenitors are also destroyed, leading to irreversible bone marrow failure. The latter challenge is overcome by the reinfusion by stem cells collected from the peripheral blood during apheresis after a stem cell mobilisation regimen consisting of non-myeloablative chemotherapy and granulocyte colony stimulating factors (G-CSF). After collection, these stem cells are cryopreserved after the addition of the cryoprotectant DMSO in liquid nitrogen. These stem cells can normally be safely stored under the appropriate conditions for more than 30 years without loss of viability.

About 24-48 hours after patients have received their high-dose bone marrow ablating chemotherapy, the stem cells are reinfused. They then move to specialised areas in the marrow stroma, called stem cell niches, where they start proliferating and differentiating over a period of 10 - 14 days. Engraftment is said to have taken place when certain minimum thresholds for the neutrophil and platelet counts have been crossed. During this period of severe pancytopenia, pre-engraftment patients are at very high risk of opportunistic infections and need specialised care by a multidisciplinary team in an isolated environment. Special care is given to diet, mouth care, psychological support and the early recognition and preemptive treatment of infections.

In patients who fail to achieve a complete or very good partial response after transplantation, a second or so-called tandem transplant can be considered if an adequate number of stem cells were stored initially. The role and type of maintenance therapy is still controversial and generally limited to patients who achieve less than a very good partial response.

In patients who have relapsed after an autologous SCT, a second autologous SCT, allogeneic SCT or treatment with salvage chemotherapy regimens or novel agents in a clinical trial setting can be considered.