Allogeneic stem cell transplantation

A. Nagler, Israel

Multiple myeloma (MM) is a life-threatening hematological malignancy. Allogeneic hematopoietic stem cell transplantation (alloSCT) is a very effective therapeutic modality with curative potential in patients with hematological malignancies. The therapeutic efficacy is mainly based on the alloreactive reaction of donor lymphocytes against the tumoral cells of the recipient named as 'graft-versus-tumor' (GVT) effect.The graft vs. myeloma effect is the basis of immunological strategies for treatment of MM. Autologous stem cell transplantation causes effective cytoreduction, but most patients subsequently relapse. Allogeneic stem cell transplantation (alloSCT) causes durable responses. The antitumour immunity mediated by lymphocytes of the donor achieves complete remission (CR) and molecular CR for 50% of patients with a long-term freedom from the disease and a cure for 20% to 25% of patients. Early attempts using myeloablative conditioning suffered from high, up to 50%, TRM. With a reduction of the toxicity of the conditioning and introduction of approaches applying reduced intensity conditioning, the results for alloSCT improved. However, they are still deficient because of continued disease progression and relapse after transplantation. Intense research effort concentrates on developing strategies to intensify remission and prevent relapse of MM after alloSCT. Therapeutic options for inducing anti-myeloma immunity are natural killer (NK) cell immunotherapy, amplification of immune responses by using monoclonal antibodies, tumor vaccination and bispecific T and NK-cell engagers. Genetically modified immune effector cells such as T-cells armed with chimeric antigen receptors (CAR) or transduced with engineered T-cell receptors with anti-tumor specificity are another exciting emerging field of immunotherapy against myeloma.