

The Use of Graft Engineering in Allogeneic Transplantation for Myeloid Malignancies

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Abstract

Although methods for engineering of allogeneic stem cell grafts are available for decades, the use of manipulated vs. unmanipulated grafts is still mainly dependent on the policy of individual centers. In transplantation regimens using engineered grafts not only the manipulation of the graft itself, but also the additional use of other transplant components and the impact of modifications of the conditioning regimen must be taken into consideration. The most frequently used technique for graft engineering remains T-cell depletion for GvHD prophylaxis, now mostly performed by positive selection of CD34+ cells. With the currently available techniques, e.g. with the Clinimacs device (Miltenyi) a highly effective reduction of T-cells with high recovery rates of CD34+ cells can reproducibly be achieved. For compensation of the reduced graft versus leukemia effect different strategies are used. Donor lymphocyte infusions are given after T-cell depleted transplants either prophylactically, based on the monitoring of hematopoietic chimerism or of minimal residual disease. With incremental doses of T-cells infused, the risk of inducing severe GvHD can be reduced and the strategy has been shown to be effective especially in CML. Several groups have started to use HSV-tk gene transduced lymphocytes for better control of severe GvHD by the potential to induce suicide of the T-cells with gancyclovir. This approach is highly attractive in concepts using manipulated stem cell grafts although recent findings have caused a debate on its efficacy and safety. The use of manipulated grafts can further be influenced by the choice of the conditioning regimen. The application of radiolabeled antibodies in addition to the conventional conditioning increases the antileukemic activity and may allow to utilize the advantage of better GvHD control with T-cell depleted transplants in diseases where the GvL effect is less active than in CML, e.g. in high risk AML.
