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Haploidentical Transplantation in Children: Update and further Prospects

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With the introduction of the concept of alloreactive Natural Killer (NK) cells based on their expression of Killer immunoglobulin-like receptors (KIR), haploidentical transplantation might offer a fascinating way to utilize their anti-leukemic effect without Graft-versus-Host Disease (GvHD). It is not clear, however, how the optimal haploidentical donor should be selected. In addition to HLA typing of donor and recipient for the prediction of NK-alloreactivity, direct determination of the donors' KIR repertoire by PCR of flow cytometry can be utilized. In a retrospective analysis of patients undergoing a haploidentical transplantation with CD34+ positive selected stem cells, we could demonstrate that NK alloreactivity determined by the direct determination of the donors' KIR repertoire predicts the risk of relapse more accurately than the donors' and recipients' HLA typing. In contrast to previous reports, a KIR/HLA mismatch was associated with a lower risk of relapse in patients with acute

lymphoblastic leukemia. Since it is not clear whether CD34+ positive selection is superior to CD3-negative depletion, we have initiated an haploidentical transplant protocol which randomizes patient either to positive selection or negative depletion using the Clinimacs device. In addition, we have initiated a clinical protocol for haploidentical transplantation of patients with either refractory malignant diseases or for second transplants after relapse after a previous myeloablative allogeneic BMT. Since these patients are at high risk of Transplant-Related Mortality (TRM), we use Reduced Intensity Conditioning (RIC) in combination with CD3-depleted mobilized haploidentical PBSC preferentially from a NK-alloreactive donor based on the direct determination of the KIR repertoire. The first clinical results in 18 patients, including engraftment, immunoreconstitution, incidence of infections and preliminary outcome data will be discussed.