TBI CONTAINING REGIMENS FOLLOWED BY HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACUTE LYMPHOBLASTIC LEUKEMIA OF CHILDHOOD

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Acute lymphoblastic leukemia in childhood is the domain of chemotherapy giving rates of event free survival of up to 80% for the vast majority of children. Only 6% of well defined high risk patients during frontline treatment but on the other side the majority of children following relapse do not have a satisfying chance of cure by chemotherapy alone. The controversy persists, whether hematopoietic stem cell transplants provide a superior chance of cure. The answer can only be given by clearly defined prospective studies including patients with the intention to transplant but finally events before the transplant can be performed. The BMF group is currently conducting such a study during frontline therapy. Out of 3050 children with newly diagnosed ALL 197 patients fulfilled the criteria for a matched related bone marrow transplantation. An acceptable family donor was available in 53 children, which is in the expected range of 27% of HLA-identical siblings or family members in Germany. Only 30 children have been transplanted at the end, using a conditioning regimen of fractionated TBI (6 x 2 Gy) and VP16 (60mg/kg). Although the transplanted children have an EFS of about 70% and the whole group with a donor and the intention to transplant of about 60% compared to 30% EFS in the complementary group, the transplant group is by far too small lead to furtherincrease of survival in the whole group of children with ALL. Some children received alternative conditioning regimens with obviously less chance of cure. But the major question for the future remains the donor availability for high risk frontline patients but more important for relapse patients in order to prove the transplant approach in general in such patients. Clearly autografts seem not to give any advantage in these type of children, unless any new approach of maintenance/immunotherapy is providing a significant additional effect. Unrelated grafts on the other side might be one option but still require a significant reduction of treatment risks, which are currently still in the range of 30-50% compared to 10% and less in matched related transplants. Cord blood transplants especially in children may be superior to adult marrow or peripheral blood stem cell transplants. And finally, first steps have been done now to overcome the high rejection rate of mismatched related grafts by increasing for example the stem cell dose and thus offering another source of stem cell grafts also for ALL patients. Unfortunately, also these transplants are still associated with high transplant related risks. Almost all centers employing haploidentical stem cell transplants are using TBI containing regimens even with an increased dose. Our own approach on this fields is to understand the side effects of conditioning regimens containing TBI on the homing process of stem cells in the microenvironment of the marrow, and to overcome ex vivo as well as in vivo such critical dysfunctions with the aim to ensure engraftment and limit transplant risks by accelerating the hematopoietic and lymphopoietic reconstitution. This model will be discussed.