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Historically, the best results of allogeneic hematopoietic transplantation have occurred with an HLA identical sibling donor. The risks of graft rejection, GVHD, and treatment-related mortality increase with greater genetic disparity between donor and recipient. Recent advances have markedly improved results with transplants from alternative donors. In this issue of Blood, Brunstein et al report parallel, multicenter, phase 2 studies evaluating unrelated cord blood or related haploidentical transplants.

The initial advance in this area was the development of unrelated donor registries. At this time more than 18 million potential donors can be accessed worldwide. The best results have been achieved with HLA A, B, C, and DR matched transplants using high resolution (allele level) typing, with results similar to those achieved with matched sibling donors.

Because of the tremendous polymorphism of the HLA gene complex, an HLA-matched unrelated donor can only be identified for about half of patients. Patients are most likely to match an individual from the same ethnic background, and those with rare alleles or linkages, and those from minority or mixed ethnicities are unlikely to have a matched unrelated donor available. Another limitation is the time necessary to conduct the unrelated donor search and organize collection from the donor.

Umbilical cord blood is a rich source of hematopoietic stem cells. Cord blood lymphocytes are less likely to produce GVHD than hematopoietic cells from adult donors. Cord blood transplants can be successfully performed from unrelated units matched for 4 or 5 HLA A, B, and DR antigens. A cord blood unit provides a relatively low stem cell dose, which results in a slower pace of hematopoietic and immune recovery. Results are improved with higher cell doses and better HLA matching. An international network of cord blood banks has been developed that can provide adequately matched cord blood units for most patients. Recent studies involving fludarabine containing preparative regimens and transplantation of 2 cord blood units to increase the stem cell dose have been reported to improve outcomes. Centers focusing on this approach have reported results similar to those obtained with adult matched unrelated donor transplants.

Another donor option is haploidentical relatives. Parents, children, and half of siblings are haploidentical, so these donors are readily available for most patients. Several centers have reported success with transplantation of T-cell–depleted peripheral blood progenitor cells with a low rate of GVHD, but these transplants are associated with a high rate of rejection, slow immune recovery, and a substantial risk of treatment-related mortality, so few centers actively pursue this strategy.

Ludick et al reported a novel approach using unmodified haploidentical bone marrow transplantation with posttransplantation treatment with cyclophosphamide, tacrolimus, and mycophenolate; this regimen produces a low rate of severe acute and chronic GVHD and treatment-related morbidity/mortality.

The Blood and Marrow Transplant Clinical Trials Network simultaneously performed 2 multicenter, phase 2 studies evaluating these promising approaches, double cord blood transplantation, or haploidentical bone marrow transplantation; the results are reported in this issue. The studies had similar eligibility criteria and used a similar nonmyeloablative preparative regimen. The 1-year cumulative incidences of nonrelapse mortality and relapse after cord blood transplantation were 24% and 31%, respectively, and 7% and 45% after haploidentical bone marrow. Each study reported 1-year survival in more than half of the patients. As independent phase 2 studies, the results cannot be directly compared. These studies do confirm that successful transplants can be performed in children and adult recipients from either unrelated cord blood or a haploidentical related donor. Further studies are required to directly compare these strategies and to optimize results of hematopoietic transplantation from every donor source. Importantly, these studies demonstrate that an adequately matched cord blood or haploidentical donor can be identified for nearly every patient; thus it is possible to provide a hematopoietic transplantation for all patients in need.

REFERENCES


Now everyone has a donor for HSCT

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