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Alternative donor transplantation for adults with acute leukemia

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Allogeneic hematopoietic cell transplantation (HCT) from a matched related donor (MRD) is the preferred therapy for many adults with acute leukemia. Yet most patients do not have matched siblings, and the numbers who do will continue to drop as the average number of children per couple in the United States continues to decline. Recent reports show little difference in the outcomes of matched related and matched unrelated transplants for acute leukemia. Additionally, survival rates at 3–5 years after transplant appear to be generally similar following matched related, matched unrelated, single antigen mismatched unrelated, double cord blood and, perhaps even after haplo-identical transplants. Nevertheless, there are differences between stem cell sources that should be considered in the choice of donor. The following review provides some perspective on the identification of the best stem cell sources for patients who do not have matches within their families.

Introduction

Based on the results of numerous prospective clinical trials and meta-analyses of these trials, allogeneic hematopoietic cell transplantation (HCT) from a matched related donor (MRD) is the

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; GVHD, graft versus host disease; HCT, hematopoietic cell transplantation; MMURD, mismatched unrelated donor; MRD, matched related donor; MURD, matched unrelated donor; TNC, transplantation nucleated cell.

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preferred therapy for many adults with acute leukemia. Table 1 provides a list of categories of patients for whom MRD allogeneic HCT should be considered according to American Society for Blood and Marrow Transplantation guidelines [1–4]. However, only a minority of patients has matched siblings, and as the average number of children per couple in the United States continues to drop, this minority will become smaller. The following discussion provides a brief summary of the alternatives for adult patients with acute leukemia but without matches within their family. Other reviews are also available [5–7].

Donor availability

Current estimates are that approximately 30% of patients with acute leukemia will have a matched sibling available to provide stem cells [8]. In another 2%–3%, a single antigen mismatched family member may be found. While data using contemporary typing methods are limited, survival following transplantation for acute leukemia using single antigen mismatched family members appears similar enough to those following MRD HCT that such donors can be used interchangeably [9]. This still leaves approximately two-thirds of patients without a matched or single antigen mismatched family member to serve as a donor. The likelihood of finding an 8/8 matched unrelated donor (high resolution matched at HLA-A, HLA-B, HLA-C, and HLA-DRB1) varies by race and ethnicity, both because of differences in representation in the unrelated donor pool but also because of differences in the degree of polymorphisms within groups. As shown in Table 2, the likelihood of finding an 8/8 matched unrelated donor (MURD) is approximately 75% for Caucasians, 35% for Hispanics, and 18% for Blacks [8]. If 7/8 matched unrelated donors were acceptable, these numbers would increase to roughly 90%, 75%, and 70%, respectively. While there is some variability in the definition of acceptable cord blood products, current protocols generally allow up to a two antigen mismatch between the cord blood unit and the recipient, and if a single unit is used a pre-cryopreservation cell dose of 2.5×10^7 total nucleated cells (TNC)/kg of recipient weight is required, whereas if double cord transplantation is planned, each cord must have a minimum of 1.5×10^7 TNC/kg. Using these criteria, adequate cord blood products exist for >90% of patients, regardless of race or ethnicity. And if haplo-identical transplants are considered acceptable, donors can be found for >95% of patients.

Comparative outcomes of matched related donor (MRD) and matched unrelated donor (MURD) HCT following ablative conditioning

Studies from both single institutions and from transplant registries have compared the outcome of MRD and MURD transplants for acute leukemia following ablative conditioning regimens. Results published in the late 1990s found a higher failure rate with unrelated donor transplants, particularly in those with early stage disease, primarily because of higher treatment-related mortality [10]. However, more recent reports show little difference in the outcomes of matched related and matched unrelated transplants for acute leukemia. For example, in a two institution study comparing the outcome of 204 MRD recipients with that seen in 152 MURD transplants following ablative conditioning in Seattle and

Table 1
Indications for allogeneic HCT for patients with acute leukemia.

Acute myeloid leukemia
1. Primary induction failure
2. First remission other than good risk disease
(good risk = *t*(8; 21), inv(16), or normal cytogenetics with double mutated CEBPA, or normal cytogenetics with NPM1+/*FLT ITD*−)
3. First relapse/second remission
Acute lymphoblastic leukemia
1. Primary induction failure
2. First remission, all categories age <35
3. First remission, Ph+
4. First relapse/second remission