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The role of second transplants for leukemia

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Second transplant

A B S T R A C T

Management of relapsed leukemia following allogeneic transplantation is challenging. Intensive chemotherapy, donor lymphocyte infusions (DLI), or second transplantation have some value, but most reported series describe only a limited number of patients surviving beyond 2 or 3 years following relapse. Additionally, understandable selection-bias of reports describing the outcomes of intensive management approaches for relapsed leukemia confound generalizability to a broader population. However numerous reports suggest that second allogeneic transplantation for relapsed leukemia following an initial transplant may produce extended disease control and survival for patients with favorable performance status, remission at the time of second transplant, and most importantly a long interval between initial transplant and relapse. Reduced intensity conditioning for second allografts may be preferable and little data exists to suggest that a new donor will improve disease control by inducing a stronger graft-versus-leukemia effect. Improved measures to prevent the first relapse, however, may protect more patients and produce a greater fraction enjoying extended leukemia-free survival.

Introduction

The rigors of allotransplant are survivable, but only control acute leukemia for 40%–70% of allograft recipients depending on the cytogenetic and molecular risk, phenotype, and remission status of the patients. Relapse after allotransplant generally leads to poor survival with only 10%–20% of patients surviving beyond 2 years [1–7]. Notably however, patients receiving intensive chemotherapy

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supplemented with either donor lymphocyte infusion (DLI) or second transplants can have improved survival over those receiving supportive care alone [6,8–17]. Survival after relapse is inferior in those with circulating blasts at relapse, active infections, or other complications. Second transplant approaches using sibling, unrelated donor (URD), or umbilical cord blood (UCB) transplantation have been reported to have similar outcomes [1,2,9,18–28].

Second transplants are sometimes performed for incomplete donor chimerism with an additional infusion of hematopoietic stem and progenitor cells to boost engraftment. They can also be used as treatment for graft failure, but reconditioning plus a second graft infusion is essential and only successful for a minority. Most second transplants, however, are done for relapse (Table 1).

In a large Center for International Blood and Marrow Transplant Research (CIBMTR) analysis of AML relapsing after allografts, only 23% of 1788 relapsed patients survived more than a year post relapse [1]. However, longer survival was associated with later post first transplant relapse (Fig. 1). Five-year survival from relapse was nearly 40% for those relapsing beyond 3 years and 30% for those relapsing 2–3 years after initial allograft. These results were not significantly influenced by patient age, suggesting that disease risk characteristics dominated the outcome. Multivariate analysis confirmed improved survival for those relapsing beyond 2 years, whether treated with DLI or a second allograft. Second transplant success may be similar with matched related donors or unrelated donors, but reported experience with haploidentical donor transplantation for second allografts is scant.

Same or different donor

It is often postulated that changing donors for a second allograft may be favorable with hopes of inducing a more potent graft-versus-leukemia (GVL) effect. An earlier CIBMTR and more recent

Table 1
Second allogeneic transplant: settings and reasons.

Settings	Rationale
Incomplete donor chimerism	Infusion to boost engraftment
Graft failure	Reconditioning + infusion for engraftment
Relapse	Provides reconditioning and restores GVL

GVL, graft versus leukemia.

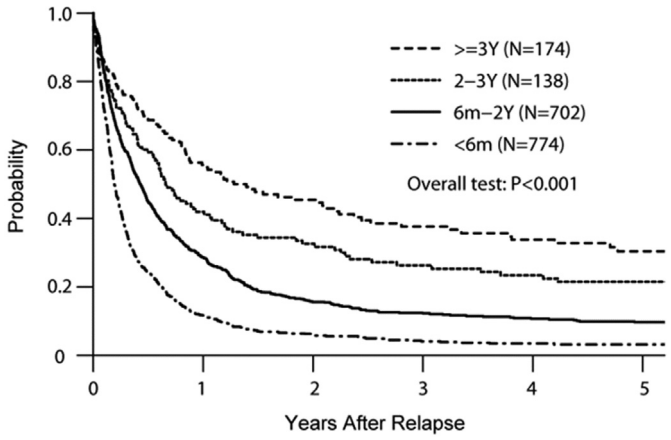

Fig. 1. Survival following relapse after allogeneic HCT for AML. Longer survival with later relapse (from Bejanyan et al., 2015 [1]).