IIE 1. Transplantation for PNH; single centers experience. Data was analyzed on 67 patients from the cited literature with special attention to eliminating duplicate reporting of patients. Of these 67 patients, 7 were transplanted from a syngeneic twin donor. Of these 7 syngeneic transplants, 4 were transplanted without conditioning, and these 4 either failed to engraft or relapsed post-transplant. Others have used a marrow ablative conditioning regimen before SCT from twin donors (n=3) of whom one showed evidence of relapse. This limited data set suggests that a marrow ablative conditioning regimen is necessary before syngeneic transplantation to prevent relapse or graft failure.

Among the 60 patients who underwent an allogeneic transplant, 47 were transplanted from an HLA-identical sibling, 1 from a haploidentical family member and 12 from an unrelated donor. Forty-seven patients received a myeloablative conditioning that was irradiation-based in 20 (34%) and busulfan-based in 14 (24%). Seven patients (12%) with PNH/aAA underwent conditioning with cyclophosphamide/ATG. The other 6 patients received various conditioning regimens. The follow-up period of patients transplanted after a myeloablative conditioning ranges from few months to over 15 years.

Most recently the use of non-myeloablative (NMA) conditioning has been advocated (n=13 patients) using either fludarabine and 2 Gy total body irradiation (n=7) or the combination of fludarabine and cyclophosphamide (n=5). The follow-up period for these patients is too short to draw meaningful conclusions about efficacy, however, graft-versus-host disease (GvHD) has been observed.

For the patients who received either myeloablative or NMA conditioning, the indication for transplantation appeared to be mainly aAA in 60% of the cases and mainly hemolysis/thrombosis in 40% of the cases. Acute GvHD of grade II or more was reported in 37% of the cases and was, as expected, the major cause of death. From all the studies analyzed, 75% of the patients were reported to be alive at last follow-up (months to years). Only one publication provided a Kaplan-Meier analysis. In that study, overall survival at 5 years was...
estimated to be 58 +/-13%. This figure is less favorable than the survival estimate of ~75% generated by combining the data from the other reports. The difference may be due to reporting bias, with centers not reporting small numbers of patients with bad outcome. The updated results from the Hospital Saint Louis (Paris, France) on 29 patients who underwent transplantation either form an HLA-identical sibling donor (n=18) (HLA-id sibling) or from an unrelated donor (UD) (n=11) are shown (Fig. 6) (G Socie and E Gluckman, unpublished data, December 2003).

IIE 2. Transplantation for PNH; Registries studies. The outcome of 57 consecutive allogeneic bone marrow transplants for PNH reported to the IBMTR between 1978 and 1995 was analyzed in 1999. The 2-year probability of survival in 48 recipients of HLA-identical sibling transplants was 56% (95% confidence interval 49%-63%), and the median follow-up was 44 months. Two recipients of syngeneic marrow transplants remained alive 8 and 12 years after treatment. One of seven recipients of alternative donor allogeneic transplants is alive 5 years after transplant. The most common causes of treatment failure were inadequate engraftment (n=7) and infections (n=3). Sixteen were grafted for PNH/aAA. The incidence of acute GvHD of grade II or more was 34%, and that of chronic GvHD of 33%.

Preliminary, unpublished analysis from the database of the EBMT (H Schrezenmeir, A Tichelli and G Socie for the SAA working party of the EBMT) on 121 patients revealed the following: Most of the patients (80%) were transplanted from an HLA-identical sibling donor; their median age at transplant was ~30 years old; the interval between diagnoses and transplant was 2.5 years. The overall survival at 10 years was 56% (95% confidence interval 46%-66%) with no statistical difference between transplants from HLA-identical sibling donors and alternative donors. Somewhat disappointing was the similar outcome per transplant period (from 1980 to 2002), showing no real improvement over an observation period of more than 20 years. Univarient analysis showed better outcome in younger patients (less than 30 years of age), and in patients transplanted less than 2 years from the date of diagnosis. As expected,
acute GvHD strongly influenced the outcome with survival over 70% in patients with acute
gvHD of grade 0-I, 63% in patients with grade II, but roughly 10% in patients with grade III-IV.
References


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