European Society for Blood and Marrow Transplantation

Severe Aplastic Anemia Working Party

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HSCT in severe congenital neutropenia

F. Fioredda *et al*.

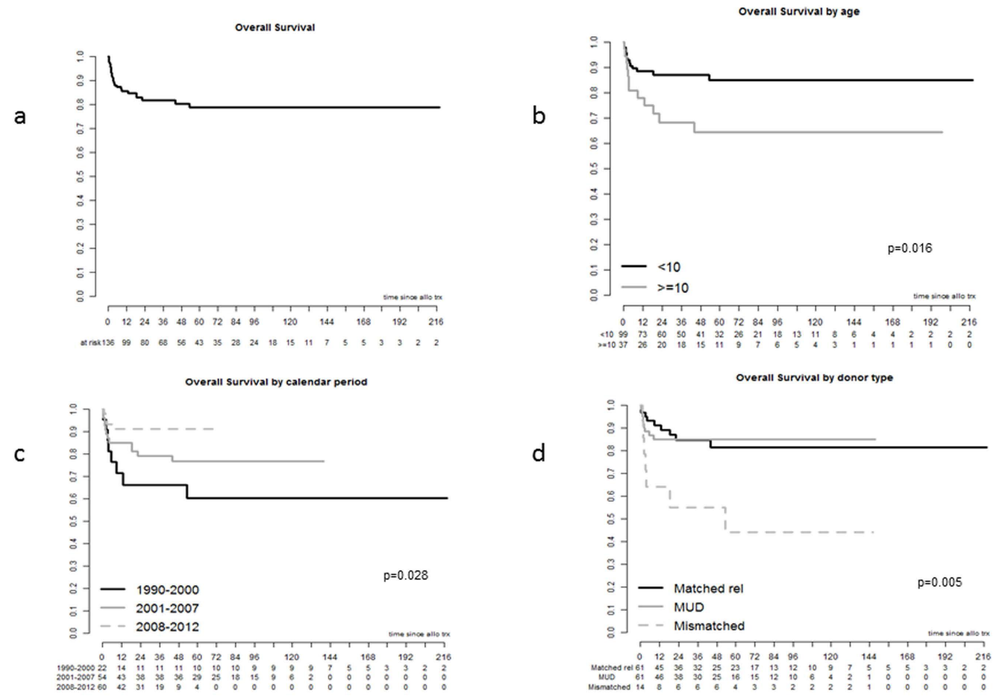

Figure*: OS curves. (A) OS. (B) OS by age. (C) OS by calendar period. (D) OS by donor type. The curves in panels C and D are shown for the maximal follow-up and were not statistically analyzed past the point of <5 patients. Mismatched includes both related and unrelated donors.*

Aim + methods: outcome of allogeneic hematopoietic stem cell transplantation (HSCT) has been studied in 136 patients affected with severe congenital neutropenia between 1990 and 2012 in European and Middle East Centres.

Results: the 3-year overall survival (OS) was 82%, and transplant related mortality was 17%. Transplants performed below the age of 10 years, in recent years and from HLA matched related or unrelated donors were associated with a significantly better OS. Moreover, in multivariate analysis HLA matched related donor and prophylaxis with ciclosporin A and methotrexate were associated with lower occurrence of acute GvHD. No secondary malignancies occurred after a median follow up of 4.6 years.

Conclusion: the outcome of HSCT for SCN from HLA-matched donors in patients younger than 10 years is acceptable. Nevertheless, the mortality is not negligible so far; a careful selection of HSCT candidates should be undertaken.

Second allogeneic HSCT for aplastic anaemia

S. Cesaro *et al.*

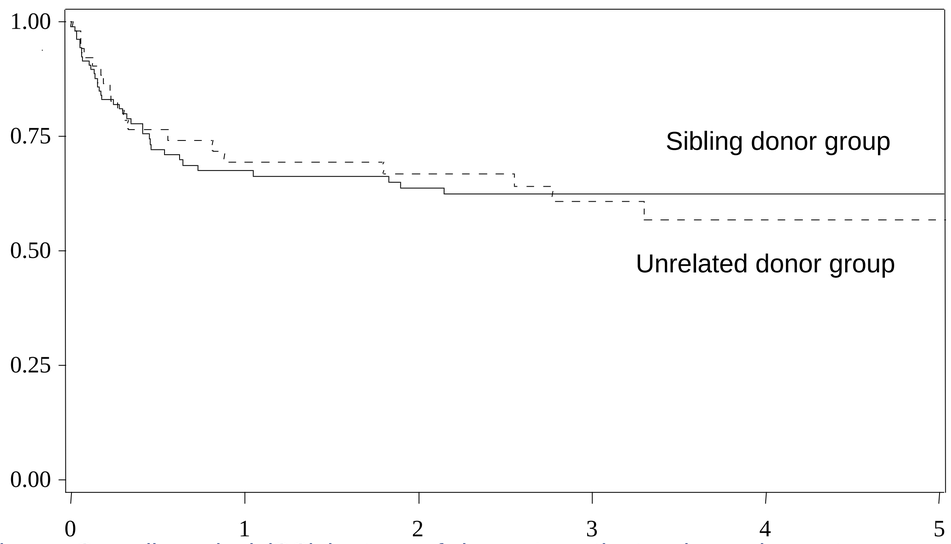

Figure*: Overall survival (OS) by type of donor. In patients who underwent a second HSCT, no difference was found according to the origin of the donor: 56·8% (95% CI 39·8–70·7) for unrelated donor group versus 62·4% (95% CI 51·7–71·4) for sibling donor group HSCT, P = 0·9. OS for the whole group was 60·7% (51·7, 68·4).*

Aim + methods: the outcome of a second allogeneic transplant (HSCT) in 162 patients, treated in the EBMT centres from 1998 to 2009, was assessed. A sibling or an unrelated donor was used in 110 and 52 transplants, respectively.

Results: the same donor as for the first HSCT was used in 81% of transplants while a change in the choice of stem cell source was reported in 56% of patients, mainly from bone marrow to peripheral blood. The stem cell source was bone marrow in 31% and peripheral blood in 69% of transplants. Neutrophils and platelets engraftment occurred in 85% and 72% of patients, after a median time of 15 days and 17 days, respectively. Grade II-IV acute graft versus host disease (GVHD) and chronic GVHD occurred in 21% and 37% of patients, respectively. Graft failure (GF) occurred in 42 patients (26%). After a median follow-up of 3.5 years, the 5-year overall survival (OS) was 60.7%. In multivariate analysis, the factor significantly associated with a better outcome was a Karnofsky/Lansky score > 80 (higher OS).

Conclusion: a second HSCT is a feasible rescue option for GF in SAA with a successful outcome in 60% of cases.

Outcome of aplastic anaemia in children

C. Dufour *et al.*

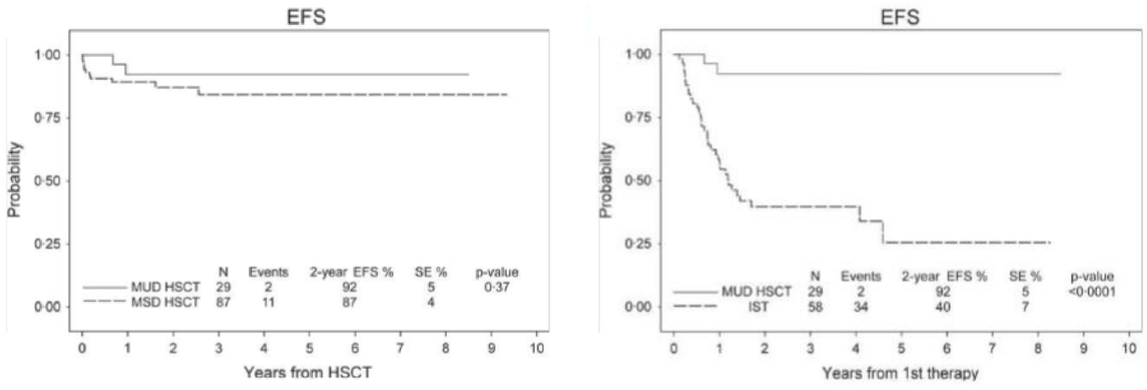

Figure*:* Kaplan-Meier curves of event-free survival (EFS). Left: outcomes following upfront-unrelated donor HSCT are similar to matched sibling/family donor HSCT in childhood severe aplastic anaemia. (sAA). Right: EFS following upfront-unrelated donor HSCT is superior to immunosuppressive therapy (IST) with lymphoglobulin and ciclosporin in childhood sAA.

Post upfront MUD/MMUD HSCT (n=29) and MSD HSCT (n=87). MUD, matched unrelated donor; MMUD mismatched unrelated donor, MSD, matched sibling/family donor.

Aim + methods: outcome of 563 Aplastic Anaemia (AA) children aged 0-12 years reported to the EBMT, according to treatment received were analysed.

Results: overall survival (OS) after upfront human leucocyte antigen-matched family donor (MFD) HSCT or immunosuppressive treatment (IST) was 91% vs. 87% (P 0·18). Event-free survival (EFS) after upfront MFD HSCT or IST was 87% vs. 33% (P 0·001). Ninety-one of 167 patients (55%) failed front-line IST and underwent rescue HSCT. The OS of this rescue group was 83% compared with 91% for upfront MFD HSCT patients and 97% for those who did not fail IST up-front (P 0·017). Rejection was 2% for MFD HSCT and HSCT post-IST failure (P 0·73). Acute graft-versus-host disease (GVHD) grade II-IV was 8% in MFD graft vs. 25% for HSCT post-IST failure (P < 0·0001). Chronic GVHD was 6% in MFD HSCT vs. 20% in HSCT post-IST failure (P < 0·0001).

Conclusion: MFD HSCT is an excellent therapy for children with AA. IST has a high failure rate, but remains a reasonable first-line choice if MFD HSCT is not available because high OS enables access to HSCT, which is a very good rescue option.

In Vivo T cell depletion strategies within HSCT for idiopathic aplastic anaemia

S. Samarasinghe *et al.*

Aim + methods: Compare the outcome of 1837 AA patients transplanted in EBMT centres in the period 2000-2013, comparing different strategies of anti-T cell serotherapy: i. no serotherapy; ii ATG; iii. Alemtuzumab.

Results: Acute GvHD was significantly lower in both ATG (13%) and Alemtuzumab (7%) patients as compared with no serotherapy (19%)(p,0.001 for both); among the 2 serotherapy, the aGvHD rate was lower in the Alemtuzumab group (p=0.012). Alemtuzumab was also more effective in the prevention of chronic GvHD (see figure on the left).

The use of serotherapy is associated with a significantly better overall survival.

Conclusions: the use of serotherapy significantly reduces the risk of both acute and chronic GvHD. Considering the fact that the composite endpoint of “GvHD-free survival” should be the goal of a HSCT procedure (even more for a non-malignant disease such as AA), Alemtuzumab should be recommended as preferred serotherapy in the context of HSCT for AA.

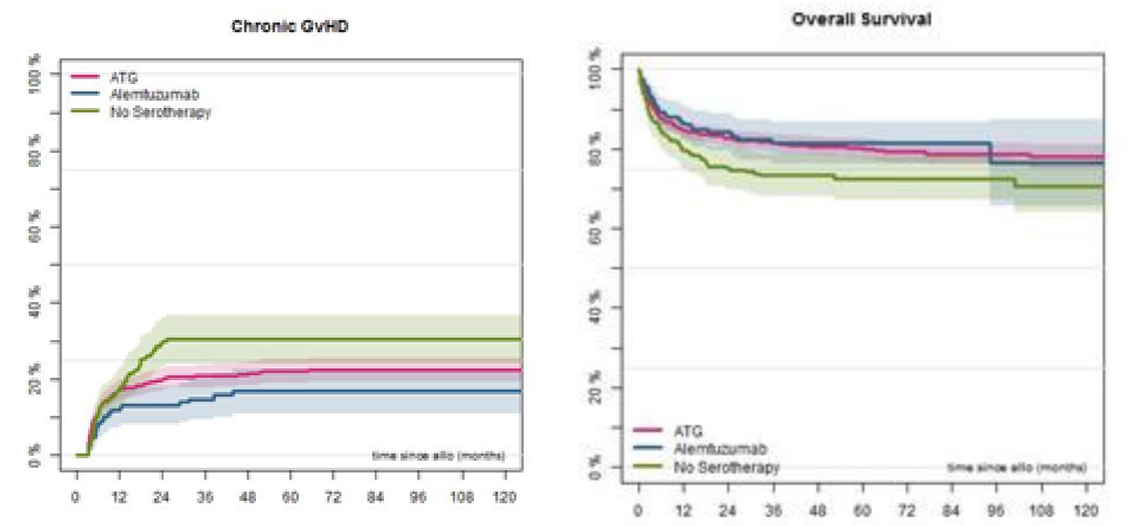

Figure: *comparing ATG and Alemtuzumab on outcomes following HSCT for aplastic anaemia.* Left: *CI of chronic GvHD. Chronic GvHD was significantly lower in both ATG and Alemtuzumab patients as compared with no serotherapy (p=0.021 and 0.003); among the 2 serotherapy, the difference in favour of Alemtuzumab was borderline (p=0.087).*

Right*: Overall survival. OS was significantly better in both ATG and Alemtuzumab patients as compared with no serotherapy (p=0.001 and 0.025); among the 2 serotherapy, there is no difference in terms of OS (p=0,604)*