Severe Aplastic Anemia Working Party

Chair: Carlo Dufour (Genova)

Secretary: Régis Peffault de Latour (Paris)

Study coordination: Cora Knol-Bout (Leiden)

Introduction Bone Marrow Failure Registry

The Working Party for Severe Aplastic Anemia (SAAWP) of the European society for Blood and Marrow Transplantation (EBMT) is a European network, started almost 4 decades ago, which has produced a number of clinical trials in the diagnostic and therapeutic development of SAA. The database of the SAA of the EBMT contains data on about 13.000 patients with different subtypes of BMFs **(tables below)** thus offering a unique opportunity for investigating many different critical aspects of these diseases (immunosuppressive treatments as well as hematopoietic stem cell transplantation), aiming to finally improve quantity and quality of survival of these patients. Within this framework the SAAWP of the EBMT continues to run a multi-national database to collect all European BMFs, combining this retrospective work with some prospective studies which aim to address further improvement in the complex treatment of these disorders.

Acquired BM failure syndrome	n
Aplastic anemia	9,642
Pure red cell aplasia (non cong. PRCA)	134
Paroxysmal nocturnal haemoglobinuria (PNH)	540
Pure white cell aplasia	10
Ameg. thrombocytopenia (non cong.)	43
Other	224
unknown	116
TOTAL	**10,593**

Genetic BM failure syndrome	n
Fanconi	1,624
Diamond-Blackfan (cong. PRCA)	223
Shwachman-Diamond	47
Dyserythropoietic anemia	27
Dyskeratosis congenita	76
Ameg. thrombocytopenia (cong.)	74
other	121
unknown	13
TOTAL	**2,192**

Unrelated donor HSCT upfront in children

Carlo Dufour & Sujith Samarisinghe

Background

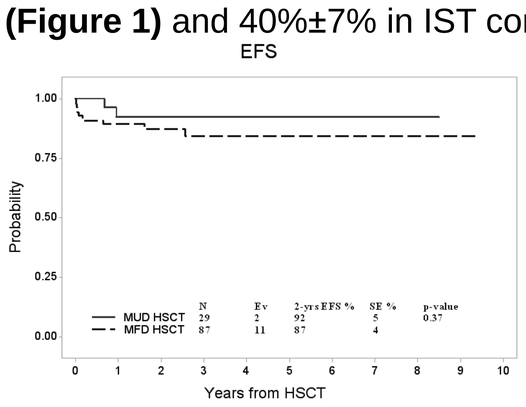
First-line treatment for pediatric idiopathic Severe Aplastic Anemia (SAA) is a matched sibling donor (MSD) hematopoietic stem cell transplant (HSCT). Most children lack a MSD and thus receive immunosuppressive therapy (IST). We explored for the first time the feasibility and safety of unrelated donor HSCT upfront in children without prior IST.

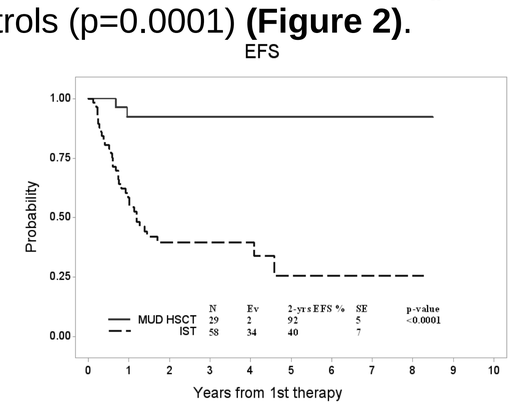
Methods

Data was collected retrospectively on twenty-nine consecutive children from 9 UK pediatric centres, who all lacked a MSD but underwent unrelated donor HSCT upfront, without prior IST. This cohort was then compared to matched historical controls who had undergone first-line therapy with a MSD HSCT (n=87) or IST with horse ATG and ciclosporin (n=58) or second-line therapy with unrelated donor HSCT post failed IST (n=24).

Results

Outcomes were excellent in the upfront HSCT cohort. The 2 year OS was 96%±4% compared to 91%±3% in the MSD controls (p=0.30) and 94% ±3 % in the IST controls (p=0.68). The 2 year EFS in the upfront cohort was 92%±5% compared to 87%±4% in MSD controls (p=0.37) **(Figure 1)** and 40%±7% in IST controls (p=0.0001) **(Figure 2)**.





Conclusion

Outcomes for upfront unrelated donor HSCT in pediatric idiopathic SAA were similar to MSD HSCT and superior to IST. MUD HSCT can be considered as first-line therapy in selected paediatric patients who lack a MSD.

Ongoing Prospective Clinical Trials

EMAA

Efficacy and Safety of Eltrombopag in Patients with Acquired Moderate Aplastic Anemia (EMAA):
a Prospective Randomized Multicenter Study comparing Thrombopoetin-Receptor agonist Eltrombopag (Revolade®, GlaxoSmithKline) with Placebo in Patients with Acquired Moderate Aplastic Anemia.

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RACE Study

Efficacy and Safety of Eltrombopag in Patients with Acquired severe Aplastic Anemia:
a prospective Randomized multicenter study comparing horse Antithymocyte globuline (hATG) + Cyclosporine A (CsA) ± Eltrombopag as front-line therapy for severe aplastic anemia patients.

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Ongoing non-interventional & Retrospective studies

The SAAWP is leading numbers of studies including:

- Non-interventional & retrospective studies of ATG vs Alemtuzumab based conditioning regimens (S. Samarasinghe)
- Definition of partial remission (A. Rovo)
- Outcome of HSCT post failed IST (H. Schrezenmeier)
- Retrospective study or survey of RIC haploidentical HSCT for refractory SAA using post graft high dose cyclophosphamide (J. Passweg & F. Ciceri)
- Recognition of Truly Refractory Severe Acquired Aplastic Anemia (A. Rovo)
- HLA-DPB1 and DRB3/4/5 matching in the context of AA and unrelated donor transplantation (R. Devillier)
- Joint study on 'secondary' autoimmune diseases following allogeneic HSCT for aplastic anemia. Together with the Autoimmune Diseases WP (P. Miller)
- Outcomes of stem cell transplantation for acquired pure red cell aplasia (S. Halkes)
- Hematopoietic Stem Cell Transplantation in severe congenital neutropenia (F. Fioredda)

CALL FOR DATA

Aplastic anemia in association with a **lymphoproliferative neoplasm** (A. Rovo)
Outcome of stem cell transplantation in **congenital dyskeratosis** (F. Fioredda)

Publications

Outcome of aplastic anemia in adolescence: a survey of the Severe Aplastic Anemia Working Party of the European Group for Blood and Marrow Transplantation.
Dufour C, et al / **Haematologica** 2014 Oct;99(10):1574-81

Outcome of allogeneic stem cell transplantation for patients transformed to myelodysplastic syndrome or leukemia from severe aplastic anemia.
Hussein AA, et al / **Biol Blood Marrow Transplant**. 2014 Sep;20(9):1448-50

Cyclophosphamide in severe aplastic anemia?
Peffault de Latour R. / **Blood** 2014 Oct 30;124(18):2758-60

SAAWP Data Office

For participation in, or information on SAA studies, please contact the SAAWP at the EBMT Data Office in Leiden, The Netherlands: SAAwpEBMT@lumc.nl.