40th Annual Meeting of the European Society for Blood and Marrow Transplantation; Milan, 30 March–2 April

EMBT calls for innovation through cooperation

The launch of defibrotide (Defitelio), the first licensed treatment for severe hepatic veno-occlusive disease after haematopoietic stem cell transplantation, has been hailed as a model for cooperation between investigators, international scientific societies and industry.

According to European Society for Blood and Marrow Transplantation (EBMT) President-Elect Professor Mohamad Mohty: 'This collaboration on an innovative drug shows how scientific societies can work with pharmaceutical companies to develop very effective products. In rare life-threatening diseases such as veno-occlusive disease, only close partnership with all interested parties can lead to success.'

An endothelial modulator, defibrotide is approved in Europe for the treatment of severe hepatic veno-occlusive disease in haematopoietic stem cell transplantation patients aged over 1 month.

In a multicentre trial, defibrotide significantly increased survival by 52% at 100 days after transplantation in patients with severe veno-occlusive disease compared to historical controls (38.2% *vs* 25.0%; *P*=0.0341). Complete response 100 days after haematopoietic stem cell transplantation was seen in 23.5% of patients receiving defibrotide *vs* 9.4% of the historical control group (*P*=0.013). Treatment with defibrotide was generally well tolerated, with a similar rate of adverse events in the two groups.

'We believe defibrotide provides a novel and life-saving option for patients, addressing an otherwise unmet medical need in veno-occlusive disease. Development of defibrotide has been driven by the physicians involved with the strong support of the EBMT. Without this support, I do not think we would be able to celebrate the drug's approval,' commented principal investigator Dr Paul Richardson, Dana-Farber Cancer Institute, Boston, USA.

Each year, about 60 000 stem cell transplants are performed worldwide, including over 3600 in the UK. Veno-occlusive disease affects around 14% of patients undergoing haematopoietic stem cell transplantation, and mortality in severe veno-occlusive disease is over 80% in both adults and children.

Defibrotide is recommended by EBMT guidelines, by the British Society for Blood and Marrow Transplantation and the British Committee for Standards in Haematology.

Sue Lyon

Dr Paul Richardson, Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Boston

Research round-up, by Sue Lyon

Upfront unrelated donor transplantation: an option in severe aplastic anaemia

A matched unrelated donor haematopoietic stem cell transplant with no prior immunosuppression may be considered for children with severe aplastic anaemia who lack a matched sibling donor. Thus concluded a retrospective analysis of outcomes in 27 UK children who underwent upfront matched unrelated donor and mismatched unrelated donor haematopoietic stem cell transplant for idiopathic severe aplastic anaemia between 2000 and 2013.

Overall survival at 2.5 years was 95.7% (95% confidence interval 72.9–99.4%) and event-free survival was 92.11% (95% confidence interval 71.9–98.0%). One child died as a result of idiopathic pneumonia syndrome at 11 months, and primary graft failure occurred in one patient with a mismatched unrelated donor haematopoietic stem cell transplant.

At last follow up, the remaining 25 patients had engrafted and 24 had normal blood counts. Grades I–II acute graft *vs* host disease occurred in 10 patients and grade III–IV in two patients.

Bhatnagar N et al (2014) Upfront matched and mismatched unrelated transplantation in paediatric aplastic anaemia: a United Kingdom multicentre retrospective experience. Abstract PH-O004

Low-dose rATG improves outcomes in children with haematological malignancies

An open-label, prospective, multicentre study reports that low-dose rabbit anti-thymocyte globulin (rATG) reduces stem cell transplant-related mortality and improves disease-free survival in children, without increasing the risk of acute and chronic graft *vs* host disease or recurrence of leukaemia.

Researchers randomized 172 patients (mean age 9 years) to either high-dose rATG (30 mg/kg) or low-dose rATG (15 mg/kg), both given at days 4, 3 and 2 before haematopoietic stem cell transplantation. After a median of 32 months, cumulative incidence of transplant-related mortality was 21% in the high-dose and 10% in the low-dose rATG group (*P*=0.06). Disease recurrence did not differ between the two groups at 17%.

Five-year disease-free survival was 59% and 76% respectively for children given high- and low-dose rATG (*P*=0.03).

Locatelli F et al (2014) Results of an open-label, prospective, randomised clinical trial on two different dosages of rabbit anti-thymocyte globulin (rATG) in children with haematological malignancies given allogeneic HSCT from an unrelated volunteer. Abstract PH-O002