Phase I study offers hope for haemophilia B treatment

Symptoms improved significantly in adults with haemophilia B following a single treatment with gene therapy developed by researchers at St. Jude Children's Research Hospital in Memphis, US and demonstrated to be safe in a clinical trial conducted by UCL (Nathwani et al, 2011).

The findings of the six-person phase I study mark the first proof that gene therapy can reduce disabling, painful bleeding episodes in patients with haemophilia B. The research was presented on 11 December at the 53rd annual meeting of the American Society of Hematology in San Diego, USA.

Four study participants stopped receiving protein injections to prevent bleeding episodes after undergoing the therapy and have not suffered spontaneous bleeding. Several have also participated in marathons and other activities that would have been difficult before gene therapy.

'This is a potentially life-changing treatment for patients with this disease and an important milestone for the field of gene therapy. It could have ramifications for the treatment of haemophilia A, other protein and liver disorders and chronic diseases such as cystic fibrosis,' said Dr Amit Nathwani of the UCL Cancer Institute, Royal Free Hospital, University College Hospital and NHS Blood and Transplant.

Each patient received a one-time infusion of the adeno-associated virus 8 vector into a vein in the arm. Two patients each were treated with escalating doses of the vector. Following treatment, factor IX levels rose in all six patients from less than 1% of normal levels before gene therapy to between 2 and 12%.

Factor IX levels increased the most in the two study volunteers who received the highest dose of the vector. After treatment, protein levels ranged from 3 to 12%.

Chief Executive of the Haemophilia Society, Chris James said: 'The Haemophilia Society has been following this research into a gene therapy for haemophilia B with great interest.

'The Society is delighted to see world-class research in the UK which may ultimately provide therapies to improve the life of those with haemophilia showing such positive results at this stage. These are early days and all medical and scientific developments need to go through extensive testing for efficacy and side effects. As such we would not wish to raise false hopes at this stage. However we hope that this research will eventually result in the removal of the need for regular injections and significantly reduce painful bleeds and debilitating joint damage for those living with haemophilia.'

Nathwani AC, Tuddenham, EGD, Rangarajan S et al (2011) Adenovirus-Associated Virus Vector–Mediated Gene Transfer in Hemophilia B. *N Engl J Med* 10 Dec [Epub ahead of print]

Depression common and long-lasting after acute lung injury

Depressive symptoms and impaired physical function were common and long-lasting during the first 2 years after acute lung injury, according to a study from Johns Hopkins University School of Medicine (Bienvenu et al, 2011). Depressive symptoms were an independent risk factor for impaired physical function.

A total of 186 mechanically ventilated patients with acute lung injury were followed up at 3, 6, 12 and 24 months following injury. Outcome measures included the Hospital Anxiety and Depression Scale (a score ≥8 indicating depressive symptoms), and dependencies in instrumental activities of daily living (two or more impairments indicating impaired physical function).

The cumulative 2-year incidence of depressive symptoms among the 147 patients without baseline depression was 40%, and the cumulative incidence of impaired physical function among the 112 patients without baseline impaired physical function was 66%. Incidence rates were highest at 3-month follow up and declined thereafter.

Bienvenu OJ, Colantuoni E, Mendez-Tellez PA et al (2011) Depressive symptoms and impaired physical function after acute lung injury: a 2-year longitudinal study. *Am J Respir Crit Care Med* Dec 8 [Epub ahead of print]

Rituximab improves survival in mantle cell lymphoma

Results of a UK phase III trial presented at the 53rd annual American Society of Hematology conference in San Diego show that the addition of rituximab (MabThera) to chemotherapy in the treatment of newly diagnosed patients with mantle cell lymphoma significantly increases survival by 8.3 months (P<0.03). This allows patients to live an average of 45.7 months compared to the 37.4 months achieved by chemotherapy alone.

Mantle cell lymphoma is currently an off-label use of rituximab, but this large trial, illustrating prolonged survival for patients suffering this potentially fatal blood cancer, will provide the necessary data for clinicians to apply for access to rituximab in this setting through the Cancer Drugs Fund.

The Secretary of State for Health, Andrew Lansley MP, announced in October 2011 that the Cancer Drugs Fund should provide access to medicines in situations such as this.

'These data represent a significant overall survival benefit to newly diagnosed mantle cell lymphoma patients. These findings suggest that we should alter the way in which we currently think about treating patients in this setting,' said Dr Simon Rule, Consultant Haematologist, Derriford Hospital, Plymouth, who was the lead investigator in this trial. 'The strategy of using MabThera in combination with chemotherapy provides the hope of extending life, for more patients than has ever been achieved before, with this potentially fatal disease.'