BOOSTB4: A clinical study to determine safety and efficacy of pre- and/or postnatal stem cell transplantation for treatment of osteogenesis imperfecta

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Objectives (all parts max 100 words)
Osteogenesis imperfecta (OI) is a heterogeneous condition with no effective cure or treatment. Severe, but viable, forms can present in-utero. Early experience indicates that transplantation of fetal mesenchymal stem cells (MSC) before and after birth may ameliorate symptoms and reduce fracturing. In the Boost Brittle Bones Before Birth (BOOSTB4) study we aim to evaluate the safety and efficacy of pre- and/or postnatal MSC transplantation in severe viable forms of OI (types III and IV), develop rapid prenatal diagnosis based on exome sequencing of fetal cells and cell free DNA in maternal blood.

Methods
Rapid exome sequencing using a panel targeted for skeletal disorders will allow definitive in-utero molecular diagnosis of OI. In-utero transplantation in 15 cases will be compared with transplantation at 4 months in postnatal cases to determine safety for the fetus, child and mother. Outcomes include fracture frequency, growth, bone mineral density to the age of 20 months. Non-invasive prenatal diagnosis (NIPD) of OI based on analysis of cell free DNA will be developed.

Results
We have established a European network centred around hubs in Stockholm, London, Leiden/Utrecht and Berlin. Early studies have shown that rapid diagnosis of skeletal dysplasias using exome sequencing is possible. To inform further development of rapid in-utero diagnosis and NIPD we seek referrals for rapid exome sequencing and development of the NIPD panel.

Conclusions
Demonstration that prenatal transplantation improves early outcome would represent a major step forward in the management of patients with severe OI, and beyond to a range of

other inherited birth defects. The BOOSTB4 consortium welcomes clinical cases for diagnosis of OI using rapid exome sequencing or NIPD (contact l.chitty@ucl.ac.uk). The clinical trial on treatment of OI with fetal MSC pre- or post-natally will commence early in 2017 (contact Cecilia.Gotherstrom@ki.se).

Learning Objective

- The participant shall be able to understand the prognosis for severe OI, the potential for in-utero therapy and how to participate in this first in man study.

Category: Fetal medical and surgical therapy