Does vascular endothelial growth factor gene therapy safely improve outcome in severe early-onset fetal growth restriction?

From 2013-01-01 to 2018-12-31, closed project | EVERREST Website

Project details

| Total cost: | Topic(s): |
| EUR 7 766 112 | HEALTH.2012.1.4-4 - Targeted nucleic acid delivery as an innovative therapeutic or prophylactic approach |
| EU contribution: | Funding scheme: |
| EUR 5 998 984 | CP-FP - Small or medium-scale focused research project |
| Coordinated in: | |
| United Kingdom | |

Objective

Fetal growth restriction (FGR) globally occurs in 8% of pregnancies, is severe and early onset in 1:500 cases, affecting 11,000 babies annually in the EU. In most cases, reduced uterine blood flow restricts substrate delivery to the fetus causing growth to slow or cease. There is no treatment. Currently the fetus is delivered very preterm before fetal death or irreversible organ damage occurs. Affected neonates suffer intracranial haemorrhage, chronic lung disease, cerebral palsy, with heart disease and diabetes as adults; mortality is high. Recent improvements in the care of premature growth restricted neonates, means that more of them survive delivery, but at great cost. Small increases in fetal growth and gestation at birth are associated with major improvements in survival and morbidity.

Improving uterine blood flow is key and Vascular Endothelial Growth Factor (VEGF) is important to achieve this. In preclinical animal models we showed that local VEGF gene transfer to the uteroplacental circulation using adenovirus vectors increases uterine blood flow, attenuates constriction of uterine arteries and increases angiogenesis; these changes result in improved growth of severely growth restricted fetuses. This is the first clinically-applicable evidence based therapy that could improve perinatal outcome in severe early onset FGR in man.

In collaboration with an SME experienced in gene therapy trials, our aim is to complete an agreed toxicology programme, identify specific ethical issues in stakeholders, and to perform a Phase I/II study in women with severe early onset FGR at four EU centres of excellence, using interventional radiology to deliver an adenovirus vector containing the mature processed form of human VEGF-D into the uterine artery. Data on safety, tolerability and efficacy will be analysed, and used, if successful, to inform phase II and III trials of this innovative therapy, leading to the first treatment for this intractable obstetric condition.

Related information

Report Summaries

Final Report Summary - EVERREST (Does vascular endothelial growth factor gene therapy safely improve outcome in severe early-onset fetal growth restriction?)
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