Study design

The Mesenchymal Stem Cell Therapy for the Treatment of Osteogenesis Imperfecta (TERCELOI) study was registered with clinicaltrials.gov (NCT02172885) and eudract.ema.europa.eu (2012-002553-38). TERCELOI is an independent multi-center phase I clinical trial to evaluate the feasibility, safety and potential efficacy of infused sibling HLA-matched MSCs in non-immunosuppressed children with OI. Enrolled patients were the following: P01, male, 6 years 1 month of age and P02, female, 8 years and 1 month of age.

P01 was born to a healthy and non-consanguineous Spanish couple. Skeletal dysplasia was suspected at 24 weeks of gestation. Cesarean delivery was at 34 weeks. At birth weight: 1,770 g (p9, -1.4 SD), length: 39 cm (p<1, -3.38 SD), OCF: 30 cm (p3, -1.96 SD). X-ray survey showed multiple fractures involving humeri, femur, tibia, and several ribs. A genetic study confirmed the clinical diagnosis of OI. A *de novo* heterozygous missense mutation was identified in exon 16 of *COL1A1* gene: c.1031G>A (p.Gly344Asp). The patient showed blue sclera and developed dentinogenesis imperfecta. He had normal neurodevelopment, sitting unsupported at the age of 9 months. He could never achieve unaided standing up or walking due to compression fractures of the spine and limb deformity. The first orthopedic surgical intervention was performed at the age of 4.5 years and consisted of correction of bilateral tibia angulation. Compassionate intravenous treatment with biphosphonates was initiated at the age of 57days. He was treated with pamidronate until the age of 5 years and 4 months when zoledronate was prescribed instead. Spontaneous fractures or with minimal trauma and chronic bone pain have been common manifestations due to the extreme bone fragility.

P02 was the first child born to a healthy and non-consanguineous couple. Skeletal dysplasia was suspected at 34 weeks of gestation. Cesarean breech delivery was at 38 weeks of gestation. Weight: 2,820g (p 33; -0.44 SD). OFC: 33 cm (p28; -0.4 SD). OI was suspected at birth. She had blue sclera, micrognatia, short lower limbs and fracture

of one clavicle. X-ray skeletal assessment showed low bone density and prenatal fracture of the contralateral clavicle, 8th rib and unilateral cubitus. Genetic studies identified a *de novo* heterozygous variant in the *COL1A2* gene: c.2133+6T>A resulting in the skipping of exon 35. At the age of two months, the patient revealed severe generalized osteopenia, and angulation of both femur and tibia with several areas of sclerosis. Compassionate treatment with pamidronate was initiated at the age of 15 month until the age of 7 years and 10 months when zoledronate was prescribed instead. She had normal social and language development. She could walk at the age of three years. Recurrent fractures of long bones of the upper and lower limbs leading to bone deformities required several surgical interventions. Mobility was largely wheelchair dependent.