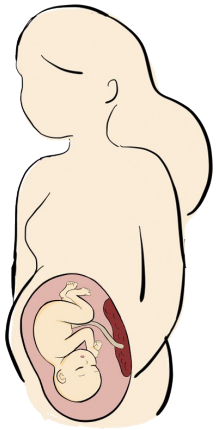
Treating Lysosomal Storage Diseases Before Birth

UCSF Benioff Children's Hospitals
Center for Maternal-Fetal Precision Medicine

Phase 1 Clinical Trial: In Utero Enzyme Replacement Therapy (IUERT) for Prenatally Diagnosed Lysosomal Storage Disorders
ClinicalTrials.gov: NCT04532047

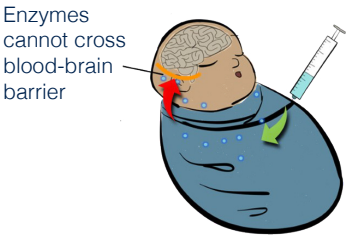
Introduction



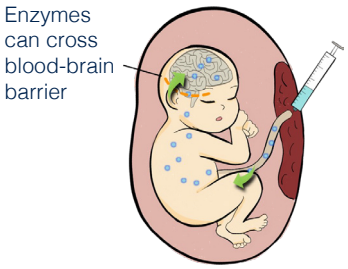
Lysosomal storage diseases (LSDs) are a group of conditions in which an important enzyme is missing. During the body's normal processes, enzymes break down material in the body to help cells function properly. When enzymes are absent, this material can build up in cells throughout the body and cause damage to organs, including the liver, brain, heart, and bones. For some LSDs the missing enzyme can be replaced. This treatment is called enzyme replacement therapy, or ERT.

LSDs can be diagnosed before or after birth. Currently, enzyme replacement is given after birth. This treatment has limits. First, patients can develop allergic reactions to the enzymes, meaning they develop antibodies against them. Second, the enzyme does not cross into the brain once the blood-brain barrier is formed, and so giving the enzyme does not stop injury to the brain. Third, damage to organs may begin before birth, and before the start of enzyme replacement therapy. This damage may not be reversed.

Injection of enzyme after birth



Fetal injection of enzymes



Lysosomal storage diseases can be devastating for patients and their families. We hope that this clinical trial will bring us one step closer to finding a definitive cure. Our mission is to give these babies and, someday, babies with similar conditions, a better life.

At UCSF, we have developed a new approach that provides enzyme replacement before birth.

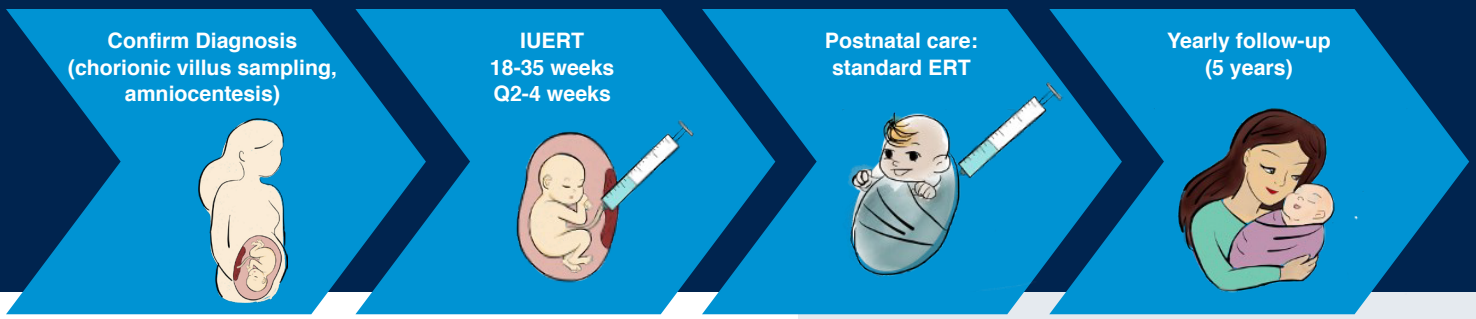
This is being studied in an FDA-approved, phase 1 clinical trial of ERT before birth for patients with specific LSDs. The trial will evaluate the safety of ERT for the fetus, the mother, and for the baby, once born.

The goal of this approach is to improve the lives of patients with lysosomal storage diseases. By giving enzyme before birth, we hope to overcome the limits of current care. In this new treatment, we inject the ERT into the umbilical vein of the fetus. This is done by placing a needle through the mother's abdomen and into the umbilical vein. The mother's abdomen will be numbed during the procedure. This same technique is routinely used for fetal blood transfusions. In utero ERT will be performed every few weeks until the baby is delivered. After birth, the baby will continue to receive enzyme replacement treatment. The baby will also be monitored closely for their first five years to understand long-term outcomes of the fetal treatment.

Included Diseases:

- Mucopolysaccharidosis (types 1, 2, 4a, 6, 7)
- Infantile-onset Pompe disease
- Neuronopathic Gaucher disease (types 2 and 3)
- Wolman disease

With any new and unproven therapy, it is important to understand the potential risks and benefits. The potential benefits of delivering enzyme replacement before birth were tested in the laboratory and designed to address some of the issues that patients can experience with these diseases.



Steps of the Trial

It is important to note that there are risks to any new therapy, particularly one given before birth. The main risk is from placing a needle into the umbilical vein of the fetus. This procedure can lead to preterm labor or infection in the pregnant woman. There may also be unknown risks.

Diagnosis of a fetus with LSD

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Video consultation to discuss pregnancy options, risks and potential benefits of fetal therapy

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In-person screening visit at UCSF to review the study and determine whether you would like to enroll

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Once enrolled in the trial:
ERT is given to fetus via umbilical vein injection, every 2-4 weeks, up until 35 weeks of gestation (at UCSF)

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Delivery
(at UCSF or local hospital)

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Maternal video visits at 1, 3, 12 months after delivery

Child receives standard postnatal care including ERT (local provider)

Child follow-up visits at 3 months (at UCSF or locally), then yearly until 5 years old (at UCSF)

If you have questions about this study, please contact the study team fetaltreatmentcenter@ucsf.edu or 1-800-RX-FETUS.

Why Treat Before Birth

- Prevent the onset of disease: LSDs can cause severe damage to multiple organs before or shortly after birth. Treatment before birth could improve outcomes by preventing the build-up of cellular materials in multiple organs as early as possible. By giving ERT before birth, we hope to improve the survival of babies with LSDs and prevent the disease from causing damage.
- Treat the brain: Giving ERT before birth could allow us to treat the effects on the brain better. ERT that is given after birth is not able to get into the brain. However, ERT given before birth may get into the developing brain and prevent or slow the progression of the disease.
- Fewer allergic reactions: After infants and children receive enzyme replacement multiple times, they can develop allergic reactions. If enzyme replacement is done before birth, that is less likely. We believe the unique immune system of the fetus will allow us to deliver enzymes without developing serious allergies. We think that this technique may prevent allergic reactions after birth when enzyme replacement is continued; we call this tolerance.

How we can support you through this journey

- We can do a video consultation when you are diagnosed to provide non-directive counseling about your pregnancy options.
- If you decide to enroll in the trial, we can coordinate your visit to UCSF to receive ERT during the pregnancy.
- If you decide to travel to UCSF to enroll in our trial, we will provide financing for travel and the research costs of the therapy. Our team will also work with your insurance company to provide coverage for other related medical costs.

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