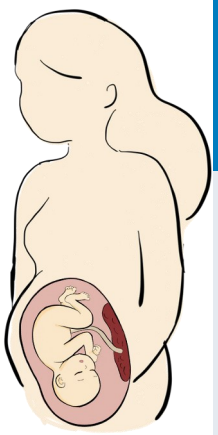
Treating Lysosomal Storage Diseases Before Birth

UCSF Benioff Children's Hospitals
Fetal Treatment Center

Enrolling Internationally

Introduction



At UCSF, we have developed a new approach to treat lysosomal storage diseases (LSDs) by providing enzyme replacement therapy (ERT) before birth. By giving enzyme prenatally, we hope to overcome the limits of current care.

Included Diseases:

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

We are studying in utero ERT in an FDA-approved, phase 1 clinical trial. **The goals** of the clinical trial are to evaluate the safety of ERT for the fetus, the mother, and infant, and to demonstrate potential benefits of treating LSDs before birth.

Our approach involves infusing the necessary enzyme through the umbilical vein of the fetus at intervals of 2 to 4 weeks, commencing between 18 to 35 weeks of gestation. This is done by placing a needle through the mother's abdomen and into the umbilical vein. The same technique is routinely used for fetal blood transfusions. During the procedure, the mother's abdomen is numbed.

After birth, the baby will continue to receive enzyme replacement treatment. The baby will be monitored closely for their first five years to understand long-term outcomes of the fetal treatment.

International Patient Registry

We have established an international registry of prenatally diagnosed patients to understand outcomes with and without in utero ERT. Contact Billie.Lianoglou@ucsf.edu (NCT05619900)

Phase 1 Clinical Trial:

In Utero Enzyme Replacement Therapy (IUERT) for Prenatally Diagnosed Lysosomal Storage Diseases

ClinicalTrials.gov: NCT04532047

We have treated three fetuses with MPS 1, MPS 2, and IOPD, and have seen encouraging results in the infants. The initial outcome from the patient with IOPD has been published in the NEJM (PMID: 36351280).

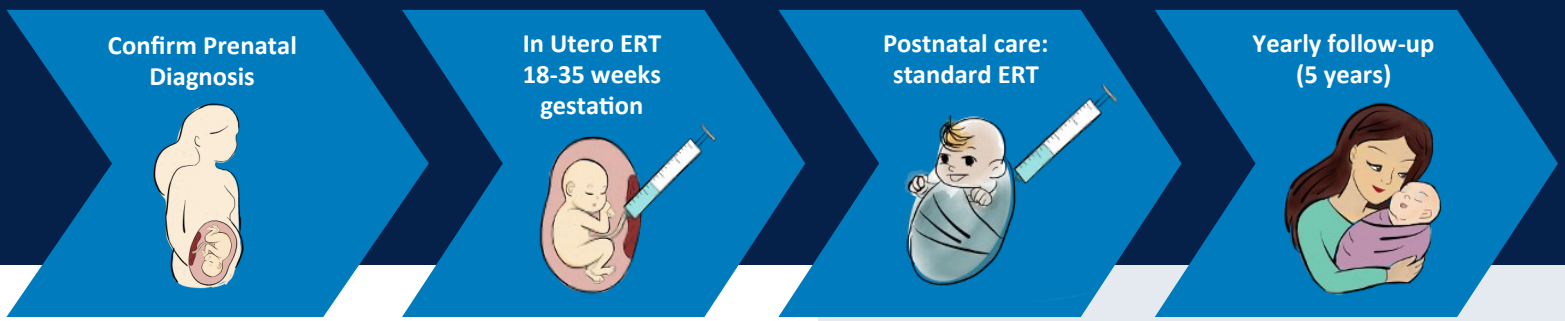
Reaching Patients

To ensure the success of this trial, we rely on individuals like you who are deeply committed to understanding these diseases and caring for families affected by them. We anticipate most trial participants will be identified in families where parents are aware of their carrier status, so your engagement as a conduit to this community is critical.

Evaluation and Enrollment Coordination

- Video consultation prior to enrollment and evaluation to provide non-directive counseling about pregnancy options.
- UCSF will coordinate travel for evaluation and ERT during the pregnancy.
- Families enrolled in this trial will incur no costs.
- **All study-related expenses, including travel costs, are fully covered.**
- The trial is sponsored by a grant from the U.S. National Institutes of Health and the UCSF Center for Maternal-Fetal Precision Medicine.

To refer a patient or ask questions about this study, please contact the study team
fetaltreatmentcenter@ucsf.edu
or 1-800-RX-FETUS



Steps of the Trial

Diagnosis of a fetus with LSD

↓

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

↓

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

↓

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)

↓

Delivery
(at UCSF or local hospital)

↓

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)

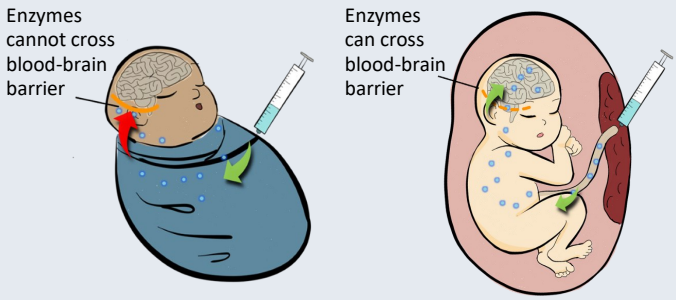
v. 8-2023

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.

Postnatal Injection of Enzyme **Fetal Injection of Enzyme**



- **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.

UCSF Fetal Treatment Center
1885 4th Street, 2nd Floor
San Francisco, CA 94158-2549
USA