Treating Lysosomal Storage Diseases Before Birth

Enrolling

Introduction

Lysosomal storage diseases (LSDs) are caused by enzyme deficiencies that lead to disabling or fatal damage to organs, including the liver, brain, heart, muscles, and bones. For some LSDs, *enzyme replacement therapy* (ERT) can replace the missing enzyme. Currently, ERT is given after birth.

UCSF has developed a new approach to treat LSDs by providing ERT prenatally to the developing fetus. This is a clinical trial of Prenatal Enzyme Replacement for Lysosomal Storage Diseases, or PEARL.

Our approach involves infusing the necessary enzyme through the umbilical vein of the fetus at intervals of 2 to 4 weeks, starting 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. The mother's abdomen is numb during the procedure.

After birth, the infant continues to receive ERT or another standard therapy. The child will be monitored closely for five years to understand long-term outcomes of the fetal treatment.

International Patient Registry

UCSF has established an international registry of prenatally diagnosed patients to understand outcomes with and without Prenatal ERT.

Contact Billie.Lianoglou@ucsf.edu

ClinicalTrials.gov NCT05619900

Pearl Trial

Prenatal Enzyme Replacement for Lysosomal Storage Diseases

FDA-approved
Phase 1 clinical trial
ClinicalTrials.gov NCT05619900

The goals of the PEARL Trial

- Evaluate safety of Prenatal ERT for the fetus, mother, and infant
- Demonstrate potential benefits of Prenatal ERT

Diseases included in the PEARL Trial

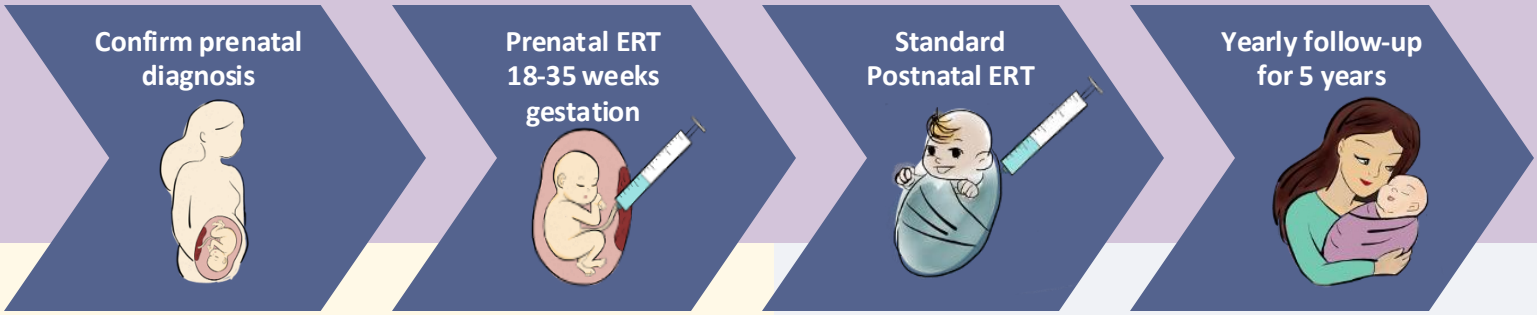
- Mucopolysaccharidosis 1, 2, 4a, 6, 7
- Infantile-onset Pompe disease
- Neuronopathic Gaucher disease (types 2 and 3)
- Wolman disease

Support for participants and families during the trial

- We offer a video consultation when you are diagnosed to provide non-directive counseling about your pregnancy.
- If you decide to enroll in the trial, we will coordinate your visit to UCSF to receive ERT during pregnancy.
- Families enrolled in this trial will incur no costs.
- All study-related expenses, including travel costs, are fully covered.
- Our team will work with your insurance company to provide coverage for other related medical costs.

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

UCSF Benioff Children's Hospitals
Fetal Treatment Center



Steps of the PEARL Trial

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, 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 (virtual)
1 year (at UCSF)

Yearly until age 5 (virtual)

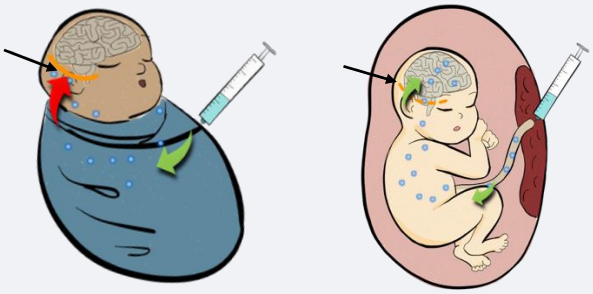
https://fetus.ucsf.edu/pearl-trial/

Why treat before birth?

- **Prevent onset of disease:** LSDs can cause severe damage to multiple organs before birth. Prenatal ERT could improve outcomes by preventing harmful build-up of cellular materials as early as possible. We think this will improve survival of infants with LSDs and prevent the disease from causing damage before birth.
- **Treat the brain:** Giving ERT before birth may allow us to better treat the effects on the brain. ERT given after birth does not circulate to the brain. Prenatal ERT can reach the developing brain and prevent or slow the progression of the disease.

Postnatal ERT
Enzymes cannot cross blood-brain barrier

Prenatal ERT
Enzymes can cross blood-brain barrier



- **Fewer allergic reactions:** Infants and children that receive ERT multiple times can develop allergic reactions to the medicine. We think this is less likely if ERT is given prenatally. We believe the unique immune system of the fetus will allow us to deliver enzymes without developing serious allergies. We think this may also prevent allergic reactions after birth when enzyme replacement is continued; we call this tolerance.

PEARL Trial
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