Primary hyperoxaluria type 1 (PH1) is an ultra-rare, inherited disorder caused by mutations in the AGXT gene that leads to the overproduction of oxalate. Oxalate is a waste product that is normally excreted by the liver and kidneys. In PH1, oxalate accumulates in the body and can cause irreversible kidney damage, leading to end-stage renal disease (ESRD) and liver disease.

# Cause of PH1

PH1 occurs when the liver enzyme alanine-glyoxylate aminotransferase (AGT) is defective, resulting in an inability to properly metabolize a metabolic byproduct called glyoxylate. This condition typically presents in early childhood and can be categorized as either type 1 (PH1) or type 2 (PH2).

# Role of oxalate in PH1

Oxalate can crystallize in the kidney, where it can form kidney stones and cause pain. These crystals can also deposit in other organs such as the liver, eyes, and brain, leading to organ dysfunction. Early diagnosis and oxalate management are crucial to preserve quality of life and avoid multi-system symptoms that are often mistaken for those of other conditions. PH1 is frequently under- or misdiagnosed.

# CRYSTALLIZATION INHIBITORS AND PYRIDOXINE

- High-dose pyridoxine (also known as vitamin B6) therapy, though PH1 has limited treatment options, is a common long-term management strategy aimed at reducing the formation of kidney stones and delaying progression over time.

- Calcium oxalate crystallization inhibitors such as alkaline citrate can help prevent the formation of oxalate crystals in the kidneys.

# ESKD is a looming threat for people living with PH1

- End stage renal disease (ESRD) often results in the need for kidney transplantation.

- Delayed graft function (DGF) is common in PH1, where the kidneys fail to function properly immediately after transplantation.

- Infections can occur post-transplantation.

- Increased fluid intake: at least 3L/day is recommended to prevent dehydration and allow oxalate to be excreted in urine.

- Extra nutritional counseling is critical.

# SEQUENTIAL OR DUAL LIVER/KIDNEY TRANSPLANTATION

- Without transplantation, PH1 patients present with ESKD and are at risk of developing severe liver disease.

- In PH1 with compromised renal function to filter out waste products, transplantation is necessary to delay the development of end-stage renal disease.

# PH1 has limited treatment options

- Current medical management strategies are aimed to reduce the formation of kidney stones and delay progression including home fluid therapy, sodium citrate, and pyridoxine.

- Ongoing research is exploring alternative treatments such as genetic editing and gene therapy to improve outcomes for people living with PH1.

# Diagnosing PH1

- Inherited disease diagnosis is currently the only effective treatment option that modifies the underlying metabolic defects associated with PH1.

- With proper diagnosis, early intervention can prevent irreversible damage to the kidneys and liver.

- It is important for families to be aware of the symptoms and signs of PH1 to ensure early diagnosis and management.

- Early intervention and monitoring are crucial to preserve quality of life and avoid multi-system symptoms.