# **ALPORT SYNDROME** FACT SHEET

## What is Alport syndrome?

Alport syndrome is a ***rare genetic condition*** characterized by kidney disease, hearing loss, and eye abnormalities. Most affected individuals experience progressive loss of kidney function, usually resulting in end-stage kidney disease. People with Alport syndrome also frequently develop sensorineural hearing loss in late childhood or early adolescence. The eye abnormalities characteristic of this condition seldom lead to vision loss.

## How many people are affected by Alport syndrome in the U.S.?

**30,000 - 60,000**
people have the disease

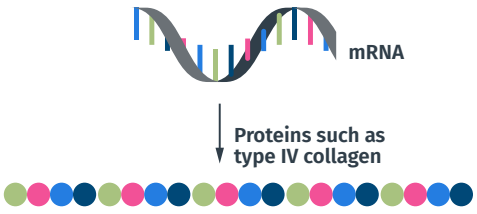
**~3%**
of children with chronic kidney disease

**~0.2%**
of adults with end-stage renal disease

**6%**
of Alport syndrome patients have a ***nonsense mutation***

## What is the cause of Alport syndrome?

Alport syndrome is caused by ***mutations in three possible genes: COL4A3, COL4A4, or COL4A5***. These genes provide instructions that code for type IV collagen protein, which play an important role in the glomeruli of the kidneys. Glomeruli are clusters of specialized blood vessels that remove water and waste products from the blood and create urine. Mutations in the genes associated with Alport syndrome ***prevent the kidneys from properly filtering the blood***. As a result, blood and protein pass into the urine. Over time, the kidneys become scarred, which leads to kidney failure.




Type IV collagen is also an important component of the Organ of Corti, the inner ear structure that transforms sound waves into nerve impulses for the brain. Alterations in type IV collagen may result in abnormal inner ear functions, which can lead to hearing loss. In addition, type IV collagen plays a role in the eye, where it helps maintain the shape of the lens and the cells of the retina. Mutations found in Alport syndrome may affect the retina and the shape of the lens.

## What are the symptoms of Alport syndrome?

The onset, symptoms, progression, and ***severity of Alport syndrome can vary greatly from one person to another*** due, in part, to the specific subtype and gene variant present. Some individuals may have a mild, slowly progressing form of the disorder, while others have earlier onset of severe complications.

- The first sign of kidney disease is blood in the urine (hematuria)
- Protein in the urine is an indication that kidney disease is progressing
  - Progression is marked by gradual loss of kidney function, frequently associated with high blood pressure
  - Ultimately, patients progress to end stage renal disease

**References:** National Institutes of Health Genetic and Rare Disease Information Center; National Organization for Rare Disorders; Division of Nephrology Washington University School of Medicine

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## Is Alport Syndrome inherited?

***Alport syndrome can be inherited in 3 ways.***

- ***About 80 percent of cases are caused by mutations in the COL4A5 gene***, are inherited through the X chromosome, and are recessive, meaning only one altered copy of the COL4A5 gene is required to pass on the disorder
- In ***approximately 15 percent of cases, Alport syndrome results from mutations in both copies of the COL4A3 or COL4A4 gene*** and is inherited when both parents carry the mutation
- Alport syndrome is ***rarely inherited as an autosomal dominant condition*** in which only one copy of a mutation is necessary to pass on the genetic trait

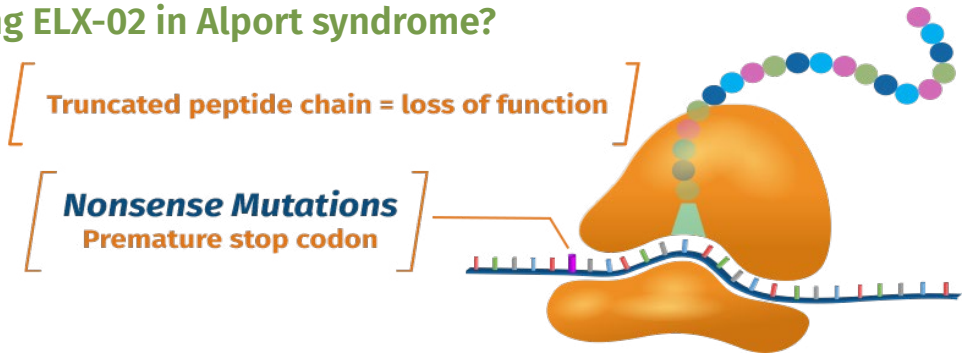
## How is Alport syndrome treated?

There are ***no approved treatments for Alport syndrome; however, current treatments are designed to address symptoms in individuals***. Some empirical evidence suggests anti-hypertensives, including angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), can be used in children at high risk of developing renal failure. Several factors must be considered before starting the therapy, such as baseline kidney function, family history, and specific symptoms present. ACE inhibitor therapy should be considered in all patients with Alport syndrome who have elevated levels of protein in the urine (overt proteinuria). Dialysis and kidney transplantation are also treatments for the disease.

Registries of patients with Alport syndrome allow researchers to gather information about individuals with the disease and help them better understand the natural history of the disease. This information is valuable for genetic counseling, which is recommended for affected individuals and their families.

## What is the rationale for studying ELX-02 in Alport syndrome?

ELX-02 is Eloxx Pharmaceutical's investigational therapy in a category referred to as Eukaryotic Ribosomal Selective Glycosides, or ERSGs. ERSGs attempt to ***overcome genetic mutations referred to as nonsense mutations***.




Pre-clinical work suggests that ***ELX-02 can overcome the stop codon and allow for normal protein production***. Eloxx has announced plans to initiate a study of patients with Alport syndrome with the COL4A5 mutation in the second half of 2022.

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