Restoring Health, Transforming Lives Through Innovation

VARIANT PHARMACEUTICALS

Therapeutic Backgrounder: Alport Syndrome (AS)

Alport syndrome (AS) is a progressive, inherited form of kidney disease that is often associated with hearing loss and abnormalities of the eye. It is caused by genetic mutations contributing to lipid accumulation and scarring in basement membranes of the kidney (glomerulus), the inner ear (cochlea), and the eye[1]. A key feature of AS is blood in the urine (hematuria) early in life, with a progressive decline in kidney function ultimately resulting in kidney failure. Hearing loss affecting both ears occurs in late childhood or early adolescence, generally before the onset of kidney failure. Patients may also have misshapen lenses in the eyes (anterior lenticonus) and abnormal retina coloration, but these abnormalities seldom lead to vision loss.

Prognosis for patients with AS is poor[1,2] and reported statistics are based on x-linked disease (XLAS), which accounts for 85% of AS cases[2]. Blood in the urine is the most common and earliest manifestation, occurring in 95% - 100% of patients[2]. Loss of renal function progresses over time, with associated edema, proteinuria, and hypertension, which is usually detectable by the second decade of life. Hearing impairment often occurs before patients progress to end-stage renal disease (ESRD), with loss of high frequency hearing common by age 25[2]. Hearing impairment progresses to loss of lower frequency hearing, and most patients are deaf by age 40[2]. Men commonly progress to ESRD and develop eye manifestations earlier than women. Ninety percent of men and 12% of women reach ESRD by age 40[2]. Thirty percent of women with AS are in ESRD by age 60 and 40% by age 80[2]. Kidney transplant is preferred over dialysis for AS patients in ESRD since there is no recurrence of disease and outcomes are good in 97% of patients[1].

AS Market

Alport syndrome (AS) represents all geographic and ethnic groups. Although the overall incidence in the general population is unknown, data from the United States demonstrates AS accounts for 3 percent of children with ESRD and 0.2 percent of adults with ESRD[1]. The gene frequency of Alport syndrome in the United States has been estimated at 1:5,000 to 1:10,000 people, suggesting there are approximately 30,000 to 60,000 affected individuals in the U.S[1].

Current AS Treatments and Limitations

There are no disease-specific treatments for AS. Current therapy focuses on minimizing loss of protein in the urine, and preventing complications from edema, thereby stabilizing kidney function. The most common drug therapy includes diuretics for edema, ACE inhibitors and ARBs for reduction of proteinuria, other antihypertensive agents.

There is a significant unmet need for effective disease-specific treatments that can delay disease progression, prevent end-stage renal disease and hearing loss, and improve patients' quality of life.

References

1. Kashtan CE. Clinical manifestations, diagnosis and treatment of hereditary nephritis (Alport syndrome), updated December 17, 2015. UpToDate.com.
2. Saxena R. Alport syndrome, updated July 21,2015. emedicine.Medscape.com.

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