APOL1-MEDIATED KIDNEY DISEASE (AMKD)

PRESENTER

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INTRO

- AMKD is associated with rapid progression to kidney failure.
- AMKD overwhelmingly affects people of Sub-Saharan African ancestry.
- Believed to be the most significant contributor to persistent health disparities in ESRD in the U.S., disproportionately affecting (X ~3.5) African Americans compared to European Americans.

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CODE PURPOSE

- To track individuals with genetic risk-factor variants that have not yet manifested into clinically overt AMKD.
- These individuals are at much higher risk for severe and rapidly progressive kidney disease and should be both advised and monitored more closely.
- To correctly identify individuals who do have overt AMKD and may be candidates for specific therapies as they become available.

CLINICAL PRESENTATION

- The root cause of AMKD is two variants in the APOL1 gene (G1 and G2), which are predominantly found in people of Sub-Saharan African ancestry, including approximately 13% of African Americans (or about 5 million individuals).
- Two copies of either of these variants "cause a 7- to 10-fold increased risk of hypertension associated end-stage renal disease, a 10- to 17-fold increase in focal and segmental glomerulosclerosis, and a 29-fold increase in HIV nephropathy."
- APOL1 genetic variants have been associated with much of the excess risk of chronic kidney disease and ESRD, with some estimates showing that the lifetime risk of kidney disease in APOL1 dual-risk genetic variants individuals is at least 15% (versus 2% lifetime risk for European Americans).

DEVELOPMENT OF AMKD

- Not all individuals with the G1/G2 variants develop AMKD. Rather, individuals with G1/G2 APOL1 risk variants develop AMKD when genetic factors interplay with epigenetic factors. Infectious or inflammatory epigenetic factors are known to be the "second hit" required to trigger AMKD in individuals with the two APOL1 risk variants.

APOL-1 IMPACT

- The presence of two APOL1 risk variants and chronic kidney disease is associated with rapid kidney disease progression to kidney failure relative to patients without two APOL1 risk variants, including higher rates of ESRD and greater progression of chronic kidney disease irrespective of diabetes status.
- For people with non-diabetic kidney disease and two APOL1 risk variants, dialysis is initiated on average 9-12 years earlier than people without the two risk variants.

APOL-1 IMPACT, CONT.

- Researchers have estimated that AMKD accounts for meaningful proportions of the clinical presentations of certain notable categories of kidney disease in people of Sub-Saharan African ancestry, including:
  - Between 54% to 73% of presentation of focal segmental glomerulosclerosis (FSGS).
  - 62% to 79% of HIV-associated nephropathy, 23% of hypertension-associated kidney disease.
  - 7% to 25% of lupus nephritis within this sub-population.
- A rough estimate suggests that AMKD may affect as many as 800,000 people in the United States.

CURRENT TREATMENTS

- Current treatments for people with AMKD include SGLT2i therapies, RAASI therapies and other antihypertensives, diuretics, immunosuppressants and other drugs such as mineralocorticoid receptor antagonists.
- These treatments are not unique to targeting AMKD but instead target the consequences of kidney disease and are used across a range of kidney diseases to delay progression to ESRD.
- At present, there is no Food and Drug Administration approved treatment specifically targeting the underlying cause of AMKD, although there are a number of potential treatments for AMKD in clinical trials now.

BENEFITS OF A NEW CODE FOR APOL-1

- Continued development of epidemiological initiatives.
- Ongoing research into treatments targeting AMKD.
- Improving clinical practice (including prognosis, informing kidney donation decisions, supporting family planning, improving understanding of treatment options and success, and supporting quality assurance efforts related to blood pressure control and kidney disease screening).

QUESTIONS?

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