A Study of the Prevalence of Apolipoprotein L1(APOL1) Alleles Among Individuals With Proteinuric Kidney Disease Who Are of Recent African Ancestry or Geographic Origin

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• Estimate the prevalence of APOL1 genotypes among individuals with FSGS who identify themselves as being of recent African ancestry or geographic origin• Estimate the prevalence of APOL1 genotypes among individuals with other forms of proteinuric...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON51493

Source
ToetsingOnline

Brief title
Study of APOL1 in Individuals With Kidney Disease

Condition

- Renal and urinary tract disorders congenital

Synonym
Proteinuric Kidney Disease

Research involving
Human

Sponsors and support

Primary sponsor: Vertex Pharmaceuticals
Source(s) of monetary or material Support: Vertex Pharmaceuticals Incorporated

Intervention

Keyword: APOL1, Kidney Disease

Outcome measures

Primary outcome

• Estimate the prevalence of APOL1 genotypes among individuals with focal segmental glomerulosclerosis (FSGS) who identify themselves as being of recent African ancestry or geographic origin

• Estimate the prevalence of APOL1 genotypes among individuals with other forms of proteinuric nondiabetic chronic kidney disease (CKD) who identify themselves as being of recent African ancestry or geographic origin

• Estimate the prevalence of APOL1 genotypes in individuals without a documented CKD diagnosis, but with a historical eGFR of <75 mL/min who identify themselves as being of recent African ancestry or geographic origin

Secondary outcome

• Identify individuals with FSGS and 2 APOL1 risk alleles to establish a group of potential participants for current and future Vertex clinical studies

• Identify individuals with other forms of proteinuric nondiabetic CKD and 2 APOL1 risk alleles to establish a group of potential participants for current and future Vertex clinical studies

Study description

Background summary

The apolipoprotein L1 (APOL1) gene is expressed in multiple organs in humans, including the kidney.1,2 The biologic function of APOL1 is to protect against parasitic infection (Trypanosoma brucei.3 Two common sequence variants in APOL1, termed G1 and G2 (i.e., risk alleles) are commonly found in individuals of recent African or Caribbean ancestry.4, 5 G1 encodes a correlated pair of non-synonymous amino acid changes (S342G and I384M), G2 encodes a 2 amino acid deletion (N388del:Y389del) near the C-terminus- of the protein, and G0 is the ancestral allele (wild type).4,5 Different studies published over the last 10 years have shown that individuals who are homozygous or compound heterozygous for these 2 variants have an increased risk of developing proteinuric kidney diseases, including focal segmental glomerulosclerosis (FSGS), interferon-induced nephropathy,6 human immunodeficiency virus nephropathy,7 and nondiabetic kidney disease (NDKD).2
This study will screen participants with FSGS and other proteinuric nondiabetic chronic kidney diseases for APOL1 variants.
Additional studies are needed to further understand the prevalence of APOL1 genotypes in participants with proteinuric nondiabetic chronic kidney disease (CKD).

Study objective

• Estimate the prevalence of APOL1 genotypes among individuals with FSGS who identify themselves as being of recent African ancestry or geographic origin
• Estimate the prevalence of APOL1 genotypes among individuals with other forms of proteinuric nondiabetic CKD who identify themselves as being of recent African ancestry or geographic origin
• Estimate the prevalence of APOL1 genotypes in individuals without a documented CKD diagnosis, but with a historical eGFR of <75 mL/min who identify themselves as being of recent African ancestry or geographic origin

Study design

This is a study of the prevalence of APOL1 alleles in individuals who are of recent African ancestry or geographic origin. The study will enroll up to a total of approximately 2500 participants into 3 groups. Group 1 includes participants with FSGS, Group 2 includes participants with other forms of proteinuric nondiabetic CKD, Group 3 includes individuals without a documented CKD diagnosis, but with a historical eGFR of <75 mL/min. No study drug will be administered. A blood sample will be collected for APOL1 genotyping. A saliva sample will be collected for exploratory use in APOL1 genotyping assay development.

Study burden and risks

Blood Draw: When you have your blood taken with a needle, it may feel like a pinch. It can hurt for a short time, and sometimes the place where the needle was put might feel sore or look bruised. Some people may experience dizziness, upset stomach, or fainting when their blood is drawn. There is a risk of infection.

Saliva Sample: There are no known risks or discomforts from the saliva collection technique.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Willing to sign and date an informed consent form (ICF) either in-person or remotely, as applicable by local law.
2. Participants aged 12 to 65 years (inclusive).
3. Participant is of African ancestry or geographic origin, which may include but is not limited to the following: Black, Caribbean, African American, Sub-Saharan African, or LatinX (defined as a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin).
4. Participants must meet one of the below criteria:
a. Group 1: FSGS.
b. Group 2: Presence of proteinuric nondiabetic CKD (not attributable to infection, neoplasia, drugs, autoimmune disorders, or diabetes).
c. Group 3: Individuals* without a documented CKD diagnosis, but with a historical eGFR of <75 mL/min.
*Including, but not limited to first degree blood relatives (i.e., parent, full sibling, or child) of individuals with end-stage kidney disease (ESKD).
5. Proteinuria as defined by at least one of the following:
a. urine protein to creatinine ratio (UPCR) >=0.5 g/g (>=500 mg/g; >=50 mg/mmol), or
b. urine albumin-to-creatinine ratio (UACR) >=0.3 g/g (>=300 mg/g; >=30 mg/mmol), or
c. urine dipstick analysis with protein reagent strip >=1+
Proteinuria can be confirmed via:
• previously documented result if it was done within 12 months before the date of informed consent OR
• by a random spot urine sample using a dipstick test performed during screening.

Exclusion criteria

1. Participant, or close relative of the participant, is the investigator or a subinvestigator, research assistant, study coordinator, or other staff directly involved with the conduct of the study at that site.
2. ESKD, defined as being on chronic dialysis.
3. Prior kidney transplant.
4. History of diabetes mellitus.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-10-2022
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	28-07-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO Date:	18-01-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL80510.018.22