Whole-Exome Sequencing in Dutch Children with PSC

Published: 06-12-2016
Last updated: 16-04-2024

To identify disease-causing gene mutations in a Dutch cohort of PSC patients who were diagnosed before the age of 13.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON46010

Source
ToetsingOnline

Brief title
WHELP-study

Condition

- Gastrointestinal inflammatory conditions
- Hepatic and hepatobiliary disorders

Synonym
Primary Sclerosing Cholangitis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: eigen middelen

Intervention

Keyword: inflammatory bowel disease, primary sclerosing cholangitis, whole-exome sequencing

Outcome measures

Primary outcome

Identification of rare coding variants of large effect that predict early-onset

PSC

Secondary outcome

Not applicable

Study description

Background summary

Primary sclerosing cholangitis (PSC) is a severe liver disease of unknown etiology leading to fibrotic destruction of the bile ducts and ultimately to the need for liver transplantation (LTx) in young adults. When PSC develops before the age of 13 it is always associated with inflammatory bowel disease (IBD), and genetics play an important role in predisposing children to early-onset PSC. Though several PSC susceptible genes and variants have been identified, large part of the heritability for PSC is still unexplained. We aim to screen the exonic regions of all the genes in patients with early-onset PSC using whole-exome sequencing (WES) to discover novel PSC related variants and genes.

Study objective

To identify disease-causing gene mutations in a Dutch cohort of PSC patients who were diagnosed before the age of 13.

Study design

Multicenter case-control study in several Dutch hospitals with sample collection between August 2016 and July 2017.

Study burden and risks

For patients with early-onset PSC the physical discomfort associated with participation is negligible, as they will undergo routine venepunctures at regular health checks. For this study two extra tubes (2 x 10 ml) will be drawn. The healthy relatives will need to undergo one venepuncture, which would otherwise not have taken place. WES will undoubtedly solve diagnostic dilemmas; however, incidental findings (IF) that may have medical and social implications will also be discovered. Actionable IF will be disclosed to participants, unless they have opted-out on the pre-test informed consent form.

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

This study involves two groups of participants:
(1) An affected individual who developed PSC before the age of 13, and in whom PSC was confirmed with either cholangiography or liver biopsy
(2) Parents of participants of group 1 ;Eligible candidates of group 1 can have any age. Confirmation of PSC by imaging is defined as the presence of multifocal strictures, focal dilatation, or beading of the biliary tree. Histological confirmation is defined as the presence of bile duct damage, onion-skinned peri-ductal fibrosis, inflammation, portal edema or fibrosis, ductopenia, ductular proliferation, or cholestasis

Exclusion criteria

Patients with PSC due to secondary causes such as surgery, trauma, cancer or infection will be excluded from participation in this study

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-01-2017
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	06-12-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-02-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL57806.042.16