TLA Technology: a new DNA diagnostic test to sequence genes that cause the disease and detect new mutations: proof of concept study voor patients with Rendu-Osler-Weber disease.

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1. Validation - of an independent geneset - of TLA technology as a new DNA diagnostic test for complete sequencing of selected genes.2. The search for structural chromosome changes in patients with ROW disease who where tested negative for mutations...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac and vascular disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON39779

Source
ToetsingOnline

Brief title
ROW DNA test

Condition

- Cardiac and vascular disorders congenital

Synonym
Rendu-Osler-Weber hereditary hemorrhagic telangiectasia

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Hubrecht Instituut

Intervention

Keyword: diagnostics, DNA, ROW

Outcome measures

Primary outcome

See study objectives

Secondary outcome

NA

Study description

Background summary

DNA Diagnostics is important in prenatal and postnatal diagnostics. Currently there is already genetic tests for ~1300 genes in the Netherlands. *Personalized medicine*, where each patient receives tailor-made treatment based on his/her own genetic profile, is increasingly applied in the treatment of various cancers. A well-known example is breast cancer. Depending whether a patient scores positive for the human EGF receptor 2 (HER2+), the estrogen receptor (ER+) or the progesterone receptor (PR+), he/she receives the corresponding, dedicated, hormone treatment. With the uncovering of the human genome sequence and the rapid progress in the discovery of genes causing disease, the relevance of DNA diagnostics for human healthcare will only increase. The number of drugs with a so-called pharmacogenomics label, where prescription depends on the outcome of a genetic test, is expected to substantially increase in the future. Current DNA analysis strategies often still rely on PCR amplification of the coding parts (exons) of the genes of interest. For example, the analysis of the hereditary breast cancer genes BRCA1&2 genes, involves almost 200 independent PCR reactions that each are then analyzed by Sanger sequencing. It enables the detection of single nucleotide changes and small insertions/deletions (indels) in the coding parts of these genes. Additional tests, such as Multiplex ligation-dependent probe amplification (MLPA), are required to detect the possible loss of alleles. The combination of these approaches is expensive, it often takes weeks or even

months to get the results, and most importantly, the analyses are incomplete. Structural variation in the genome, such as translocations, inversions and insertions (Figure 1) are not detected by any of the current strategies used in clinical DNA diagnostics. However, they account for an estimated 5-20% of all genetic variation present in the genome. This implies that currently a substantial percentage of patients erroneously scores negative for mutations in clinically relevant genes. To circumvent this in the future, there is a need for cheap and fast technologies that provide the complete sequence of genes of interest.

Study objective

1. Validation - of an independent geneset - of TLA technology as a new DNA diagnostic test for complete sequencing of selected genes.
2. The search for structural chromosome changes in patients with ROW disease who where tested negative for mutations in an earlier test.

Study design

This study is partly blinded. The investigator of St Antonius hospital is known with the mutations within the stuydpopulation but the investigator in the Hubrecht Institute is blinded.

Study burden and risks

The test will have minor burden for Patients. Patients will have a regular bloodtest with - for the study - two extra bloodsamples (two tubes) that will be collected. There are no risks for the patients who participate.

Contacts

Public
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegien 3435CM
NL
Scientific
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegien 3435CM
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patient with Rendu Osler Weber disease who didn't have a mutation tested in the previous testmethod
Patients with known ENG or ALK mutation

Exclusion criteria

Patients without ROW

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2013
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	28-03-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL42459.100.12