Pharmacogenetic testing in the clinical setting: is screening for TPMT genotype a cost-effective treatment strategy? The first prospective randomized controlled trial within the Dutch health care system.

Published: 19-02-2007
Last updated: 20-05-2024

The objective of this project is to find out if TPMT genotyping prior to thiopurine use is cost-effective in patients with inflammatory bowel disease (IBD) in need of immune suppression.

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON30092

Source
ToetsingOnline

Brief title
cost-effectiveness of TPMT pharmacogenetic testing

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's Disease and Ulcerative Colitis, Inflammatory Bowel Disease

Research involving
Human

Sponsors and support

Primary sponsor: Zorgonderzoek Nederland (ZON)
Source(s) of monetary or material Support: ZonMW;Doelmatigheidsprogramma

Intervention

Keyword: cost-effectiveness, haematological ADRs, Pharmacogenetics, thiopurine-methyltransferase

Outcome measures

Primary outcome

Outcome measures are occurrence of ADRs, clinical outcome after 5 months of

treatment, quality of life and treatment costs.

Secondary outcome

In a second phase, after inclusion of all patients and completion of the

cost-effectiveness study the DNA and phenotype data will be used for

exploratory analyses of other genes influencing treatment response.

Study description

Background summary

Pharmacogenetics aims at providing optimized drug treatment to patients by maximizingefficacy and minimizing adverse drug reactions (ADRs) based on genetic testing. The best-established example of a pharmacogenetic test is genotyping of thiopurine S-methyltransferase (TPMT) in the treatment of patients with immunosuppressive thiopurines. The frequency of ADRs (15-50%) including life-threatening myelosuppression necessitates regular monitoring of organ function and blood counts in thiopurine users. Genetic variants of TPMT explain part of the bone marrow suppressions.

Study objective

The objective of this project is to find out if TPMT genotyping prior to thiopurine use is cost-effective in patients with inflammatory bowel disease

(IBD) in need of immune suppression.

Study design

We propose to carry out a prospective randomized controlled trial (RCT) investigating 1000 patients treated with thiopurines.The project will be carried out in 3 years, 29 months are planned for patient inclusion, data analysis and reporting of results will take place from month 25 to 36.

Intervention

Following randomization, 500 patients will be genotyped prior to treatment with the clinician receiving advice on thiopurine dosing; an equal number will receive standard treatment.

Study burden and risks

The patients will undergo an extra venapuncture, carried out by experienced personnel, which is generally a low risk procedure. They will have to use a diary for disease outcome evaluation for 1 week, keep track of their expenditures with regard to disease treatment and fill out a number of questionnaires. Furthermore, an effect on treatment outcome is possible in the intervention group, that can be started on a lower dose of thiopurine according to genotype.
A possible benefit of participation will be observed in the intervention group, in which patients can be started on a lower dose of thiopurine according to genotype, preventing myelotoxicity.
If the study shows cost-effectiveness of the pharmacogenetic test without effect on treatment outcome, the genetic test will become available for all future patients starting thiopurine treatment and will help prevent part of the myelotoxicity.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

· Age 18 or older
· Diagnosis of a form of IBD
· Patient is started on azathioprine treatment
· Patient giving informed consent

Exclusion criteria

· Previous treatment with azathioprine
· Co-prescription of allopurinol (this treatment blocks xanthine oxidase, an enzyme important for azathioprine metabolism)
· Baseline leukocyte count less then 3x10^9 per litre
· Reduced baseline liver function
· Reduced renal function at baseline
· Use of TPMT phenotype test to guide prescription
· Pregnancy or breastfeeding

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2006
Enrollment:	1000
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL13171.091.06