Dihydropyrimidine dehydrogenase (DPD) deficiency and haematological abnormalities

Published: 01-09-2017
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To establish whether or not DPD deficient patients suffer from an altered white blood cell homeostasis or function, in particular of B or T lymphocytes.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	White blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON44558

Source
ToetsingOnline

Brief title
DPD deficiency

Condition

- White blood cell disorders

Synonym
Dihydropyrimidine dehydrogenase deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Dihydropyrimidine dehydrogenase, haematology, White blood cells

Outcome measures

Primary outcome

To establish whether or not DPD deficient patients suffer from an altered white

blood cell homeostasis, in particular that of B or T lymphocytes.

Secondary outcome

To investigate the function of white blood cells from DPD deficient patients.

Study description

Background summary

Dihydropyrimidine dehydrogenase (DPD, EC 1.3.1.2) is the initial and rate-limiting enzyme, catalysing the reduction of uracil and thymine to 5,6-dihydrouracil and 5,6-dihydrothymine, respectively. DPD deficiency (MIM 274270) is an autosomal recessive disease characterized by thymine-uraciluria. In patients with a complete DPD deficiency, a considerable variation in the clinical presentation has been observed. Phenotyping of DPD knock-out mice revealed significantly decreased numbers of white blood cells and the white blood cell subset lymphocytes, indicating a homeostasis problem in B or T lymphocytes. So far, it is unknown whether DPD deficient patients also suffer from a homeostasis problem in B and/or T lymphocytes.

Study objective

To establish whether or not DPD deficient patients suffer from an altered white blood cell homeostasis or function, in particular of B or T lymphocytes.

Study design

Prospective cohort study.

Study burden and risks

There are no additional risks to the regular blood sampling and the burden

associated with participation is minimal. In case the haematological findings, as observed in DPYD KO mice, can be recapitulated in DPD deficient patients, we demonstrate that a DPD deficiency is associated with a compromised immune system, which will have consequences for subsequent surveillance both for infections and malignancies. It may be that the clinical presentation of DPD patients is more diverse than anticipated and we should search for this metabolic defect in patients with infections and malignancies as well.

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

- genetically and/or biochemically confirmed DPD deficiency

- written permission to participate to the study by the participant and/or the parents/caregivers in case of children or incompetent adults

Exclusion criteria

None

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-12-2017
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	01-09-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL62514.018.17