Personalised Therapeutics @ LUMC

Published: 21-04-2022
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To implement pre-emptive panel based PGx testing in the LUMC and determine patient benefit of PGx guided drug prescription and dispensing.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON54078

Source
ToetsingOnline

Brief title
PT@LUMC

Condition

- Other condition

Synonym
n.v.t.

Health condition

Geen specifieke aandoening, patienten worden voor een geplande opname geïncludeerd

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Health~Holland,Bio.logis

Intervention

Keyword: Adverse Drug Reactions, Implementation, Pharmacogenetics

Outcome measures

Primary outcome

The primary outcome is the occurrence of drug-genotype associated adverse drug reactions (ADR) in the first 12 months following the genetic test. The outcome is dichotomized at >= grade 3 CTC-AE.

Secondary outcome

1. The occurrence of clinically relevant (classified as NCI-CTCAE grade 3, 4, or 5) patient reported ADRs, attributable to a PGx drug, at one, three, six and twelve months of follow-up.

2. Acceptance of the recommendations measured by comparing the number of dose adjustments and medication switches in the intervention and control arm. This will provide information about the acceptance of the different health care professionals.

3. The cost-effectiveness of a pre-emptive PGx panel test will be analysed by relating healthcare costs (including genetic testing, drugs and ADR-related care) to quality-adjusted life years (estimated using the EQ-5D-5L).

4. The occurrence of clinically relevant (classified as NCI-CTCAE grade 2, 3, 4, or 5) patient reported ADRs, attributable to a PGx drug, within one year of follow-up.

5. The occurrence of clinically relevant (classified as NCI-CTCAE grade 2, 3, 4, or 5) patient reported ADRs, attributable to a PGx drug, at one, three, six and twelve months of follow-up.

6. The frequency of PGx drug prescriptions (per PGx gene) (corrected for dose

changes due to PGx outcome) within one year of follow-up.

Study description

Background summary

Pharmacogenomics (PGx) is the study of genetic variability affecting an individual*s response to a drug. PGx is a critical component of personalised medicine. Currently, PGx is applied for individual drugs and/or individual genetic variants. We recently proposed a pre-emptive panel-based approach including 48 PGx variants covering 14 genes for which the Dutch Pharmacogenetic Working Group (DPWG) has issued evidence based drug dosing guidelines. The PGx panel contains all genetic variants that are considered actionable by the DPWG i.e. requiring a dose adjustment or switch to another drug. Interestingly, more than 95% of the Dutch population carries one or more actionable genotype(s) for one of the genes covered by this panel and 10% carries 4 or more. Based upon national prescription data we estimate that 5.6% of all first prescriptions would require an individualization of the dose or drug. However, in current clinical practice the potential of PGx testing is not fully exploited and the impact for LUMC is unknown. Therefore a prospective study on pre-emptive PGx testing will be performed in the LUMC.

Study objective

To implement pre-emptive panel based PGx testing in the LUMC and determine patient benefit of PGx guided drug prescription and dispensing.

Study design

A prospective, open, randomized study in 1,000 patients with a duration of 3 years.

Patients are randomised to PGx-guided dosing or standard of care. The PGx guided group receives pre-emptive PGx testing for a panel of 14 genes (including 260 PGx variants) followed by personalised drug and dose recommendations for newly prescribed drugs. Recommendations are based on the guidelines of the Dutch Pharmacogenetics Working Group. Patients in the control group will receive usual drug prescriptions, without PGx-guided drug or dose selection. Questionnaires will be used to investigate the results of the intervention.

Substudies: We plan to conduct 3 sub-studies with the obtained data. The first

study aims to explore novel associations of genetic variants associated with drug response. The second aims to explore the impact of concomitant medication and other non-genetic factors on pharmacogenetic associations. The third aims to test if an HLA risk allele panel test could be useful to identify people vulnerable to drug hypersensitivity.

Intervention

Patients are randomised to PGx-guided dosing or standard of care. The PGx guided group receives pre-emptive PGx testing for a panel of 13 genes (including 227 PGx variants) followed by personalised drug and dose recommendations for newly prescribed drugs. Recommendations are based on the guidelines of the Dutch Pharmacogenetics Working Group. Patients in the control group will receive usual drug prescriptions, without PGx-guided drug or dose selection.

Study burden and risks

Participation in this study carries a small extra burden:
1) 10 ml blood will be collected during a venipuncture. 2) to complete an online questionnaires at one, three, six and twelve months. No extra visits to the clinic are necessary. Benefits to patients in the study arm include a potentially reduced risk of ADRs. All patients will receive their pharmacogenetic profile which can be used to individualize drug treatment based on the DPWG guidelines. Overall, minimal risks are expected for included patients due to the fact that all of the drugs included within this study have previously been licensed for routine use and thus have been evaluated as having a positive benefit/risk ratio. The DPWG guidelines are based on systematic review of the literature, have been published in peer-reviewed journals and are commonly accepted.

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

Provision of informed consent (IC) prior to any study specific procedures.
Be aged >=18
Is able to provide a blood sample via venapunction
Receive a medication verification interview
Be able and willing to be followed-up for at least one year

Exclusion criteria

Pregnancy or lactating
Previous participation in the PREPARE trial (NCT03093818, NL60069.058.16)
History of a liver transplantation or stem-cel transplantation

Study design

Design

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

Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-12-2022
Enrollment:	1000
Type:	Actual

Ethics review

Approved WMO

Date:	21-04-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	03-08-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	26-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	23-08-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL78161.058.21