Diagnosing invasive fungal infections on DNA extracted from serum or plasma of immunocompromised patients with a suspected invasive pulmonary fungal infection

Published: 30-08-2017
Last updated: 19-08-2024

1. Optimise the DNA extraction process on serum and plasma to increase the sensitivity of DNA-based fungal infection diagnostic test (especially genetic mutations conferring azole resistance in invasive aspergillosis). 2. Evaluate new targeted as...

Ethical review	Approved WMO
Status	Pending
Health condition type	Leukaemias
Study type	Observational invasive

Summary

ID

NL-OMON50191

Source
ToetsingOnline

Brief title
Aspergillus Resistance PCR Optimalization study (ARPOS-study)

Condition

- Leukaemias
- Respiratory tract infections

Synonym
invasive aspergillosis, invasive fungal infections

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Aspergillus DNA PCR, Aspergillus Fumigatus, Azole resistance, DNA extraction

Outcome measures

Primary outcome

All patients will be classified as proven, probable or possible, undetermined

or no invasive pulmonary fungal infection according to the EORTC/MSG criteria.

From the patients with probable or proven invasive aspergillosis, the number

and percentages of patients samples producing a result by two different PCRs.

Secondary outcome

Not applicable

Study description

Background summary

Invasive aspergillosis (IA) is the most common mould infection in immunocompromised patients with haematological disease, but in up to 20% of the patients other fungi like Mucorales, Fusarium or Pneumocystis cause invasive fungal disease (IFD). Voriconazole, a triazole, improves overall survival of patients with an IA and is the mainstay of therapy. Resistance of A. Fumigatus emerged as an important clinical problem and infections with azole resistant Aspergillus have a high mortality. Nowhere in the world, azole resistance is more prevalent than in the Netherlands. Rapid detection of resistance is key to improve the patient's outcome but fungal cultures take time and are often negative. We aim to improve the detection of Aspergillus as well as other moulds on serum, plasma and urine. Specifically for Aspergillus fumigatus, we aim to improve the possibility to test for azole resistance associated mutations on fungal DNA extracted directly from serum, plasma and urine. Eventually we hope that by improving the non-invasive diagnostic tests (1) fewer patients will need to undergo invasive diagnostic tests (e.g.

bronchoscopy, lung biopsy) and (2) we can accelerate the diagnostic pathway and the outcome in patients with a suspected fungal infection.

Study objective

1. Optimise the DNA extraction process on serum and plasma to increase the sensitivity of DNA-based fungal infection diagnostic test (especially genetic mutations conferring azole resistance in invasive aspergillosis).

2. Evaluate new targeted as well as metagenomic shotgun DNA sequencing-based tests able to detect a broad range of fungi.

Study design

A prospective pilot study. Blood and urine samples from immunocompromised hematology patients with a suspected pulmonary invasive fungal infection will be obtained and processed following informed consent.

Study burden and risks

Blood sample collection can cause mild discomfort such as dizziness, pain, redness or a small bruise at the puncture site. Rarely this can cause an infection. Collection of urine samples will not lead to a burden or risk for the patients.

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

*18 years or older
*Lung CT showes lesions that fullfill the EORTC/MSG radiological criterium of possible invasive fungal infection.
*A bronchoalveolar lavage is planned or has been performed <48hrs earlier

Exclusion criteria

* Unable or unwilling to provide informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-07-2017
Enrollment:	300
Type:	Anticipated

Ethics review

Approved WMO Date:	30-08-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL62004.078.17