Korte versus lange behandeling met een carbapenem voor onverklaarde koorts tijdens hoog risico neutropenie bij hematologische patiënten: een gerandomiseerde non-inferiority studie.

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Short empirical treatment with a anti-pseudomonal carbapenem in hematology patients with unexplained fever during neutropenia is non-inferior to extended treatment with regard to treatment failure.

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26213

Bron
NTR

Aandoening

Hematologic malignancy
Neutropenia
Neutropenic fever
Unexplained fever
Stem-cell transplantation
Chemotherapy

Ondersteuning

Primaire sponsor: VU university medical center
Overige ondersteuning: follows

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoint is the percentage of patients with failed treatment. Treatment failure is defined as the occurrence of one of the following events after 3x24hours of treatment with a carbapenem.
The patient:
1. Has fever at the first day of the end of the neutropenic episode (defined as the first day with neutrophil count >0.5*109/L).
2. Has experienced recurrence of fever after more than 24 hours of defervescence.
3. Is diagnosed with a clinically or microbiologically documented infection.
4. Shows signs or symptoms of septic shock (systolic blood pressure <90mmHg unresponsive to fluid resuscitation and/or oliguria <5mL/kg/hour).
5. Dies between the start of the investigational treatment protocol and recovery of neutropenia.

Toelichting onderzoek

Achtergrond van het onderzoek

Randomized clinical trial aimed at investigating whether the duration of empiric antibacterial therapy in patients with hematologic malignancies and unexplained neutropenic fever can be safely reduced. A multicenter randomized clinical non-inferiority trial comparing safety of short (3 days) vs extended treatment (9 or more days) with an anti-pseudomonal carbapenem for hematology patients receiving standard antimicrobial prophylaxis is proposed.

Doel van het onderzoek

Short empirical treatment with a anti-pseudomonal carbapenem in hematology patients with unexplained fever during neutropenia is non-inferior to extended treatment with regard to treatment failure.

Onderzoeksopzet

The investigational treatment protocol will end after any of the following events:

1. End of the neutropenic episode (ANC <0.5*109/L)

2. Diagnosis of a clinically, microbiologically documented infection after randomization.

3. In case the patient shows symptoms of septic shock (systolic blood pressure <90mm Hg unresponsive to fluid resuscitation and/or oliguria <5mL/kg/hour)

4. Death due to any cause.

5. Lack of patient compliance or withdrawal of informed consent (especially refusal to continue treatment according to protocol).

6. Major protocol violation

7. Contra-indication to administer imipenem-cilastatin or meropenem due to allergy, side effects or carbapenem-resistant microorganism(s) in a microbiological culture.

8. Recurrence of fever after defervescence after randomization.

Onderzoeksproduct en/of interventie

TREATMENT:

Patients will be included in the first 3x24hours hours after the start of antibiotic treatment and will receive standard diagnostic investigations and empirical treatment with imipenem-cilastatin 500mg QID or meropenem 1000mg TID during this period. If, intensive clinical, radiological and microbiological evaluation yields no explanation for fever, patients are eligible for randomization between 2x24 hours and 3x24hours after start of empirical antibiotic treatment. Patients will be randomized into two groups.

INFORMED CONSENT AND RANDOMISATION:

Within 72hours after onset of fever every eligible patient will be asked for informed consent. Each consenting patient is then randomized to either the short treatment arm or the extended treatment arm. This will be the start of the investigational treatment protocol.

EARLY DISCONTINUATION ARM:

In the short treatment group, imipenem-cilastatin or meropenem will be discontinued after 3x24 hours irrespective of presence of fever. If fever has resolved by this time, no further action will be undertaken. If fever persists after 3x24hours, antifungal treatment with voriconazole (or anidulafungin in case of azole-resistant fungi in surveillance cultures) will then be started after 4x24 hours and will be continued until recovery of neutropenia (ANC >0.5*109/L).

EXTENDED TREATMENT ARM:

In the extended treatment arm, the duration of imipenem-cilastatin or meropenem treatment depends on the presence of fever. Patients who are afebrile after 3x24hours after appearance of fever will continue for at least 6 more days. If fever persists after 3x24hours, antifungal treatment with voriconazole (or anidulafungin in case of azole-resistant fungi in surveillance cultures) will then be started after 4x24 hours and will be continued until recovery of neutropenia (ANC >0.5*109/L). The treatment with a carbapenem will be continued until patients have been treated for at least 9x24 hours and have been afebrile (tympanic membrane temperature <37,5°C) for at least five consecutive days or until resolution of neutropenia (ANC > 0,5 x109/L), whichever comes first.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients with malignant hematological diseases being treated with cytotoxic chemotherapy or stem cell transplantation;

2. High-risk neutropenia;

3. Fever;

4. Age 18 years or older;

5. Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Contraindications to use of imipenem-cilastatin or meropenem such as allergy, previous severe side-effects or previous microbiological cultures with carbapenem-resistant microorganism(s).

2. Corticosteroid use ≥10 mg per day prednisolone or equivalent during the previous 7 days.

3. Clinically or microbiologically documented infection.

4. Symptoms of septic shock (systolic blood pressure <90 mm Hg unresponsive to fluid resuscitation and/or oliguria (urine production <5mL/kg/hour)).

5. Previous enrollment in this study during the same episode of neutropenia.

6. Any critical illness for which Intensive Care Unit treatment is required.

7. Legal incompetency

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-07-2014
Aantal proefpersonen:	224
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing
Soort: Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3499
NTR-old	NTR3675
Ander register	NCT: 02149329 : EudraCT: 2014-001546-25 ABR: NL48960.029.14
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A