Teicoplanin as Infection Prophylaxis in Pediatric Acute Myeloid Leukemia

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Intravenous teicoplanin prophylaxis dosed 20 mg/kg/once daily three times per week with a two to three days interval is safe and effective in decreasing the occurrence of culture-proven VGS BSIs in pediatric patients with newly-diagnosed AML during...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29284

Bron
Nationaal Trial Register

Verkorte titel
Pro-Teico

Aandoening

(Pediatric) Acute myeloid leukemia

Ondersteuning

Primaire sponsor: Princess Máxima Center for Pediatric Oncology
Overige ondersteuning: The investigators have received a grant from the Dutch Foundation KiKa.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoint of the safety run-in is the number of DLTs. The primary endpoint of the

randomized phase is the (first) occurrence of a culture-proven BSI with VGS during initial AML treatment.

Toelichting onderzoek

Achtergrond van het onderzoek

Due to intensified treatment, pediatric patients with acute myeloid leukemia (AML) are at high risk of developing severe infections. In this population, Viridans Group Streptococci (VGS) are a prevalent cause of Gram-positive bloodstream infections (BSIs), which occur in about 30% of the patients. These VGS BSIs infections are associated with severe complications and may result in VGS shock syndromes, which are associated with intensive care admission rates up to 60% in some series, and mortality rates up to 20%. Nonetheless, no antibiotic VGS prophylaxis is recommended by (inter)national guidelines because of the lack of supporting evidence.

Our aims are to assess the safety of i.v. teicoplanin prophylaxis three times per week with a two to three days interval during a safety run-in, and to prospectively evaluate whether this schedule decreases the occurrence of culture-proven VGS BSIs during initial pediatric AML treatment. Additionally, a population pharmacokinetic (PK) model of teicoplanin will be constructed using this schedule.

The study is set up as a prospective, international, multicenter, open-label, randomized clinical trial, preceded by a safety run-in. Pediatric patients (0-19 years) with newly-diagnosed AML treated according to the international NOPHO-DBH AML 2012, or a consecutive protocol, are eligible. Patients will be randomized to receive either teicoplanin or no teicoplanin prophylaxis.

The primary endpoint of the safety run-in is the number of dose-limiting toxicities (DLTs) observed. The primary endpoint of the randomized phase is the (first) occurrence of a culture-proven BSI with VGS during initial AML treatment.

PK samples will be drawn from the central venous line (CVL) on different time points to determine teicoplanin serum levels.

A sample size of 122 patients (n=61 in each arm) will achieve 80% power to detect an absolute reduction of 20% VGS BSIs (that is, from a conservative estimate of 25% in the control group to 5% in the intervention group) at a significance level of 0.05 using a two-sided test for proportions. An interim analysis is considered at 75% (n=92) of evaluable patients.
The results will help to develop international evidence-based guidelines concerning infection prophylaxis during pediatric AML treatment. If the number of VGS BSIs can be reduced, this will contribute to a reduction of infection-related morbidity and ultimately mortality.

Doel van het onderzoek

Intravenous teicoplanin prophylaxis dosed 20 mg/kg/once daily three times per week with a two to three days interval is safe and effective in decreasing the occurrence of culture-proven VGS BSIs in pediatric patients with newly-diagnosed AML during initial treatment.

Onderzoeksopzet

1. End of safety run-in: number of DLTs --> completed. The data safety monitoring board did not observe any safety issue at the end of the safety run-in and recommended to continue with the trial with i.v. teicoplanin 20 mg/kg/once daily three times per week with a two to three days interval.
2. Interim analysis at 75% of enrolled patients (n=92)
3. End of RCT

Onderzoeksproduct en/of interventie

i.v. teicoplanin prophylaxis 20 mg/kg/once daily three times per week.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• Newly diagnosed with AML
• Being registered and starting treatment according to the NOPHO-DBH AML 2012 study protocol, or a consecutive protocol
• Age 0-19 years
• Written informed consent by the patient and/or legal guardians (whatever applicable according to the patients' age)

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• Acute promyelocytic leukemia
• Secondary AML
• Down Syndrome
• Preexisting primary immunodeficiency
• Patients who receive regular antibiotic prophylaxis against Gram-positive bacteria for other conditions than leukemia-related
• Patients with a history of a severe allergic reaction (CTCAE grade ≥3) to teicoplanin and/or vancomycin
• Patients with an eGFR of <30 ml/min/1.73m2 at the start of the study
• Patients with a history of severe impaired hearing (CTCAE grade ≥3)
• Pregnant or breast-feeding patients

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	20-05-2021
Aantal proefpersonen:	130
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Toelichting
After data collection and analyses, the results will be presented at (inter)national conferences in the field of pediatric oncology. After final analysis, our findings will be submitted to international peer-reviewed scientific journals.

Ethische beoordeling

Positief advies

Datum:	01-11-2019
Soort:	Eerste indiening

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	NL8130
Ander register	Medical ethical research committee of the University Medical Center Utrecht : METC 20-466

Resultaten

Samenvatting resultaten
Peer-reviewed international journals