Teicoplanin as Infection Prophylaxis in Pediatric Acute Myeloid Leukemia

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29284

Source
Nationaal Trial Register

Brief title
Pro-Teico

Health condition

(Pediatric) Acute myeloid leukemia

Sponsors and support

Primary sponsor: Princess Máxima Center for Pediatric Oncology
Source(s) of monetary or material Support: The investigators have received a grant from the Dutch Foundation KiKa.

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

Secondary endpoints include the number of BSIs with culture-proven bacteria, the number of infection-related (pediatric) intensive care admissions, the number of episodes/admissions with (neutropenic) fever, infection-free survival time, infection-related mortality, number of days until neutrophil recovery (ANC ≥0.5 x109/L following the nadir), incidence of resistant bacteria in rectal VRE swabs and in (routine) surveillance throat and rectal swabs, resistance patterns of pathogenic isolates from blood cultures, adverse events (AEs) of special interest (i.e. Grade 3 or 4 increases in serum creatinine, Grade 3 or 4 hearing impairment, Grade 3 or 4 allergic reaction to teicoplanin administration, Grade 3 or 4 sepsis with teicoplanin-resistant organisms, and the occurrence of teicoplanin-resistant organisms in routine surveillance cultures), serious adverse events, data on the use of other (i.v.) antibiotics (empirical/treatment), antifungals and antivirals, PK parameters of teicoplanin, serum creatinine levels, serum levels of teicoplanin and duration of response (time between achieving complete remission after starting study treatment and documented relapse or death), CIR, EFS and OS. Exploratory endpoints include the number of hospitalization days, costs of antibiotics and days on i.v. antibiotics.

Study description

Background summary

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.

Study objective

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.

Study design

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

Intervention

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

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Eligibility criteria

Inclusion criteria

• 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)

Exclusion criteria

• 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

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-05-2021
Enrollment:	130
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Plan description
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.

Ethics review

Positive opinion

Date:	01-11-2019
Application type:	First submission

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	
NTR-new	NL8130

Register ID

Other	Medical ethical research committee of the University Medical Center Utrecht : METC 20-466

Study results

Summary results

Peer-reviewed international journals