Research into administration of lower dosed rituximab using an injection in patients with Rheumatoid Arthritis

No registrations found.

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

Summary

ID

NL-OMON20186

Source
NTR

Brief title
RTX-SC

Health condition

Rheumatoid arthritis

Sponsors and support

Primary sponsor: Sint Maartenskliniek
Source(s) of monetary or material Support: none

Intervention

Outcome measures

Primary outcome

To investigate non-inferiority of rituximab SC 336 mg to rituximab IV 200 mg, with the lower boundary of the 95% confidence interval of AUC0-6mnd,SC : AUC0-6mnd,IV exceeding the non-inferiority margin of 0.8.

Secondary outcome

• To describe the relevant pharmacokinetic parameters of rituximab 336 mg SC compared to 200 mg IV: peak level, trough level, Cavg;
• To evaluate the between group difference in changes in disease activity (DAS28-CRP) after 6 months, compared to a NI margin of 0.6;
• To evaluate the between group differences on B-cell counts;
• To assess the differences in incidence of anti-drug antibodies (ADAs);
• To assess the incidence of AEs in both groups;
• To assess patient preferences for either SC or IV formulation.

Study description

Background summary

Rituximab (RTX) is a chimeric antibody directed at CD20 positive B-cells that is authorized for the treatment of rheumatoid arthritis (RA) in the dosage of 2x 1000 mg every six months. A large systematic review showed that low-dose RTX (1x 1000 mg or 2x 500 mg) is as efficacious for RA as this higher dose. Recently, the REDO-study has been performed, demonstrating a good response on continued treatment with even ultra-low dose RTX (1x 500 or 1x 200 mg) for a large proportion of RA patients. After dose optimization, patient friendliness and organization of care might be further improved when rituximab can be administered subcutaneously. Therefore, we want to explore the therapeutic possibilities of subcutaneous (SC) administration of ultra-low dose RTX, by performing a pharmacokinetic non-inferiority study using the already authorized subcutaneous formulation of Roche (MabThera 1400 mg solution for subcutaneous injection (120 mg/ml:11.7 ml), registered for non-Hodgkin lymphoma. Patients with RA, using RTX IV 500 or 200 mg every 6 months, with stable disease activity will be included. Previous non-response to ultra-low dose RTX or a contraindication or objection to receive either therapy are reasons for exclusion. Patients will be randomized between RTX 336 mg subcutaneous or 200 mg intravenous. Blood samples for rituximab serum levels, anti-drug antibodies and CD20+ B-cells will be drawn pre-dose, post-dose (after infusion for the IV group, 2-4 days after injection for the SC group), after 3 months and after 6 months. Disease activity using DAS28-CRP will be measured at baseline, after 3 months and after 6 months. The main endpoint of the study is pharmacokinetic non-inferiority based on AUC0-6months between RTX 200 mg intravenous and 336 mg subcutaneous.

Study objective

We expect to find pharmacokinetic non-inferiority between RTX 336 mg subcutaneous and 200 mg IV

Study design

Baseline; 3 days (SC only); 3 months; 6 months

Intervention

Rituximab 336 mg subcutaneous (MabThera 1400 mg solution for subcutaneous injection (120 mg/ml:11.7 ml); Rituximab 200 mg intravenous (Rixathon 100 mg concentrate for solution for infusion)

Contacts

Public
Sint Maartenskliniek
Celeste van der Togt

024 3272793
Scientific
Sint Maartenskliniek
Celeste van der Togt

024 3272793

Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Rheumatoid arthritis: either 2010 EULAR/ACR RA17 and/or 1987 ACR RA18 criteria and/or clinical diagnosis of the treating rheumatologist;
• Patients using rituximab in ultra-low dose: either 200 mg or 500 mg as previous dose, given every 6 months, with or without concomitant methotrexate;
• Having sufficient response to rituximab treatment, operationalized as a DAS28-CRP <2.9 3-6 months after the last infusion and/or judgment of low disease activity by the treating rheumatologist;
• ≥16 years old and mentally competent;
• Ability to read and communicate well in Dutch.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation

in this study:
• Previous non-response to ultra-low dose rituximab (DAS28-CRP > 2.9);
• Objection or contraindication to either of the treatment options;

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	04-10-2020
Enrollment:	36
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	08-09-2020
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	NL8884
Other	CMO Arnhem-Nijmegen : 2020-6779

Study results