Statistical Analysis Plan

TITLE. Rituximab (RTX) Therapy in Patients With Active TAO

NCT 02378298

Date 2024-09-30

1 STUDY DETAILS

1.1 Study Objectives

    A. Do the background variables differ between NR-RTX and R-GC or NR-GC?

    B. Does RTX lower the CAS of the non-steroid responsive TAO-patients (NR-RTX), in comparison to NR-C, that continued with iv GC, and R-GC?

1.2 Study Design

.See Protocol of the study

1.3 Treatment Groups

Treatment groups: NR-RTX and R-GC or NR-GC.

1.4 Power Calculation

No power calculation was performed due to the lack of data from any similar study of RTX in GC non-responders

2 STUDY VARIABLES

2.1 Baseline Variables

2.1.1 Demographics and Baseline Characteristics only available at baseline

- Age (years)
- Sex (man /woman = m/w)
- Smoking status (smoker/previous smoker/non-smoker)
- Previous treatment (operation/RAI/ATD)
- Current treatment (Levothyrocin/ATD)
- Time from diagnosis of GD (years)
- Duration of eye symptoms (months)

2.1.2 Laboratory/evaluation measurements only available at baseline:

- fT4 (pmol/L)
- fT3 (pmol/L)
- TSH (mIE/L)
- Exophthalmometry left (mm)
- Exophthalmometry right (mm)
- Subjective diplopia (non/intermittent/corrected with prism)

2.2 Variables evaluated throughout the study

- TRAb antibodies
- Waist circumference change (%)

- High systolic blood pressure (ja/nej)
- High diastolic blood pressure (ja/nej)
- ALT increased (ja/nej)
- AST increased (ja/nej)
- OGTT results (diabetes/glucose intolerance)
- Short ACTH test (normal/inadequate response)
- Collected information on patient-reported adverse events

2.3 Analysis Variables

2.3.1 Primary Variable

- Change of CAS (clinical activity score) between the observation timepoints and the previous timepoint: comparison between the treatment groups
- CAS: comparison between the treatment groups at the different timepoints

2.3.2 Secondary Variables

- Change of CAS between the observation timepoints and the baseline: comparison between the treatment groups
- Comparison of frequency of adverse events between NR-RTX and R-GC.
- TRAb antibodies

3 STATISTICAL METHODOLOGY

Tests between groups will be made for the NR-RTX group and all of the other groups one at a time; R-GC and NR-C (where applicable).

For continuous variables Mann-Whitney U-test will be used for analyses between two groups. For dichotomous variables Fisher exact test will be used for test between two groups. For ordered categorical variables Mantel Haenszel Chi Square test will be used for test between two groups.

For all continuous variables Wilcoxon's Signed-Rank test will be used for within group analyses.