RITUXIMAB IN LIFE THREATENING THERAPY RESISTANT PROGRESSIVE INTERSTITIAL PNEUMONITIS

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON41026

Source
ToetsingOnline

Brief title
RITUX-IP TRIAL

Condition

- Autoimmune disorders
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
auto-immune mediated insterstitial pneumonitis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: auto immune disease, interstitial pneumonitis, rare lung disease, rituximab

Outcome measures

Primary outcome

The main objective of this study is to assess the effects of rituximab as a rescue therapy for rare therapy resistant progressive IMID- IP patients. a) Our primary goals can be measured by improvement of lung function in and improvement in the quality of life (QoL).

Secondary outcome

Our secondary objectives are to assess potential predictors b) Parallel to the treatment effect we will study additional parameters to potentially predict treatment effect. The first consists of a unique rituximab scan to visualize the potential binding sites for CD20 cells (and thus rituximab treatment efficacy) and second, there are specific molecular markers assessed by blood analysis which may give additional insight in the disease. Additional objectives are to assess the cost burden of the disease: c) Cost effectiveness: these consist of the cost savings when preventing or delaying lung transplants vs. the cost of rituximab, improvement in lung function and quality of life.

Study description

Background summary

Immune mediated inflammatory diseases (IMIDs) encompass a broad spectrum of inflammatory disorders and this project will address rare IMIDs involving the lungs. When left untreated, interstitial pneumonitis (IP) can lead to poor quality of life due to worsening of the pulmonary function, ultimately leading

to an increased mortality. Due to the extreme rarity of the condition, known as IMID-IP, no large randomized trial can ever be performed. Current treatments of this disease are with various immunosuppressive drugs, however unfortunately not all patients respond. Those with advancing IP will ultimately risk respiratory failure and death. Even though lung transplantation could be a final option, this is a rare and extremely expensive procedure. Thus there is a strong demand for a new therapeutic option. Recent studies on immune mediated diseases in rheumatology and also lung inflammatory disease show encouraging results with rituximab. A clinical improvement as well as improvement of lung function has been demonstrated in a number of cases. Since rituximab effectively suppresses CD20 B lymphocytes, this gives rise to fundamental questions of the role of CD20 in inflammation. Since the study population is so rare, only an experienced and specialized tertiary referral center may provide the necessary conditions for a phase III trial with rituximab. When rituximab can stabilize disease and improve lung function this could provide the patient with a new life saving treatment option. In addition, delay or prevention of lung transplantation has significant potential for cost savings.

Study objective

The main objective of this study is to assess the effects of rituximab (RTX) as a rescue therapy for therapy resistant progressive IMID- IP patients. Specifically there is an objective assessment of (1) pulmonary function tests (PFTs) and (2) Quality of Life measurement The secondary objectives are to assess the value of (1) an innovative rituximab scan to visualize RTX target sites (2) various prognostic markers biomarkers (3) cost effectiveness of the RTX treatment

Study design

Prospective study following an interrupted time series (ITS) design.

Study burden and risks

Since there are currently no other options to treat immune mediated pulmonary inflammation, apart from waiting in the lung transplant list, the offlabel treatment with rituximab seems justifiable. Serious side effects may occur, however these are extremely rare. Furthermore we are the first study to utilize a Zr-89 immuno PET/CT scan (rituximab scan) to analyse possible patient characteristics of responders and non-responders. This is very useful in this rare disease population for future patients. This way it may become possible in the future to select patients accordingly on the basis of chances of reponse, and thereby avoiding unnecessary treatments in non-responders.

Contacts

Public
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein 3430 EM
NL
Scientific
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein 3430 EM
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age: 18 - 70 years • No previous therapy with rituximab • Diagnosis of co-existing IMID and a severe and / or progressive IP by one of the following: - Clinical symptoms consistent with interstitial lung disease between 3 months and 3 years prior to screening - FVC <50% pred. and/or DLCO <40% pred. - Diagnosis of usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), Organizing pneumonia (OP) or a mixed form of UIP / NSIP / OP by either of the following: * Open or video-assisted thoracic surgery (VATS) lung biopsy showing definite or probable UIP / NSIP / OP - HRCT scan showing definite or probable UIP / NSIP / OP / mixed - Worsening as demonstrated by any one of the following within the past year: * > 10% decrease in FVC * > 15% decrease in DLCO • Therapy resistance to 1st (corticosteroids) and 2nd line therapy (cyclophosamide, AZT) • At least 2x PFT measurements in last 6 months

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: • Residual volume >120% predicted at screening • DLco <25% of predicted value at screening • History of unstable or deteriorating cardiac or neurological disease • Pregnancy or lactation • Hematology lower than specified limits (leucocytes) • Positive HIV, hepatitis B or C serology • Pre-existing conditions which lead to a life expectancy of less than 6 months. • Receipt of any vaccine, particularly live viral vaccines, within 4 weeks before first rituximab dose. NOTE: • Fever (> 37,9 °C) at presentation is reason to delay therapy by 1 week • Evidence of active infection is reason to postpone rituximab treatment until no further signs of active infection • Severe renal impairment is not a contraindication for rituximab therapy, however if patients (might) require dialysis frequently they will be excluded from the study group.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-10-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Mabthera
Generic name:	Rituximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-07-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-10-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2013-005269-37-NL
CCMO	NL49534.100.14

Study results

Date completed:	25-10-2017
Actual enrolment:	23