Anti-Biopharmaceutical Immunization: Prediction and analysis of clinical relevance to minimize the risk of immunization in Rheumatoid arthritis patients

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PRIMARY OBJECTIVE• To find early bio-markers within 3 months of the treatment with biopharmaceuticals (BP) able to predict immunization against BP within the first year of treatment.SECONDARY OBJECTIVES• To analyze the correlation between...

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

Summary

ID

NL-OMON41266

Source
ToetsingOnline

Brief title
ABI-RA-P01

Condition

- Autoimmune disorders
- Joint disorders

Synonym
Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Innovative Medicines Initiative (IMI)

Intervention

Keyword: anti-drug antibodies, biologicals, biomarker, rheumatoid arthritis

Outcome measures

Primary outcome

Primary outcome: Measurement of antibodies agains biological after 1 year.

Study parameter: different variables will be evaluated; these techniques are still partly under construction. It involves serological, cellular, immunological and genetic markers.

Secondary outcome

Secundary outcomes:

1. secundary non-response

2. therapy related potential immunologic mediated events.

Study parameter: different variables will be evaluated; these techniques are still partly under construction. It involves serological, cellular, immunological and genetic markers.

Study description

Background summary

The introduction of biopharmaceuticals (BP) has been a critical step forward in

care for RA and 9 BP are now licensed for the treatment of RA. In spite of this progress, failure of response to BP is frequent and in most of the registries, less than 50 % of patients are still on drug at 5 years. These failures may be primary failures or secondary failures. The fact is that the low level of response becomes insufficient compared to the expectations. One of the main potential causes of these failures of BP therapy response is the development of ADAb in some patients. ADAb may decrease the efficacy of BPs by neutralizing them or modifying their clearance and they may be associated with BP-specific hypersensitivity reactions. The prediction, prevention and cure of anti-drug (AD) immunization are thus major goals in BP development.
In addition, many factors (patient-, disease- or product-related) may influence the potential risk of BP immunogenicity. Therefore, the immunogenic potential of BPs can only be definitively assessed in human studies. Furthermore, emphasis has been placed on optimizing assays designed to detect ADAb response.
This prospective study (ABI-RA-P01) will assess the occurrence of ADAb using standardized and validated assay(s) and also cellular, genetic and molecular parameters in RA patients treated with adalimumab, etanercept, infliximab, tocilizumab and rituximab, to address the mechanism of immunogenicity.
Patient-related factors that might predispose an individual to an immune response will be taken into account: underlying disease, genetic background, immune status, including immunomodulating therapy and dosing schedule.
Thus, novel approaches to characterize anti-drug lymphocytes responses will be tested in patient materials (DNA, RNA, serum, PBMC).

Study objective

PRIMARY OBJECTIVE
• To find early bio-markers within 3 months of the treatment with biopharmaceuticals (BP) able to predict immunization against BP within the first year of treatment.

SECONDARY OBJECTIVES
• To analyze the correlation between immunization to BP and hypersensitivity reactions and loss of response
• To analyze the correlation between immunization to BP and BP blood levels
• To analyze the correlation between BP levels and hypersensitivity reactions and loss of response
• To identify molecular and cellular biomarkers associated with the development of ADAb at any time of treatment
• To find predictive bio-markers before initiation of the treatment BP able to predict immunization against BP within the first year of treatment
• To be able to associate an immunological signature to patients with ADAb

Study design

This is an exploratory multicenter, prospective cohort study in patients with

RA. The study will be performed within approximately 25 to 50 centres in 4 countries, including 18 centres in France.
There will be 6 fixed study visits. The visits will be done according to standard clinical practice with additional blood sampling.

Duration of study participation for each patient
• Screening : From 1 to 4 weeks
• Sampling period(s) : it will be the same for the 4 studied BPs
- M-5 to D0 (Screening)
- M0/W0/D0 (Baseline)
- M1/W4 ± 2W
- M3/W12 ± 2W
- M6/W26 ± 2W
- M12/W52 ± 4W
• End-of-study : At W52 after all the scheduled study procedures (e.g. blood sampling) and after agreement by the investigator or sub-investigator
• Total study duration: 52 weeks

Study burden and risks

Since the BP therapy will be prescribed by the Treating Physician this study is not an intervention trail. Therefore, the pre-screening of patients for administration of BP therapy and safety follow-up will be done according to national guidelines for BP*s. This will be the responsibility of the Treating Physician.
The procedures of this study are;
1) gathering clinical data
2) drawing of blood for further analysis
Blood drawing has a relatively low risk of adverse reactions.
Due to the fact that this study is accompanied with a small risk of adverse reactions we do not expect serious adverse reactions to occur.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male and female patients of more than 18 years old diagnosed with RA according to 2010 ACR/EULAR criteria
- Patient for whom the Treating Physician has decided to prescribe in the usual manner in accordance with the terms of the marketing authorization and independently from entry into this study:
• Adalimumab, etanercept, infliximab, infliximab biosimilar, rituximab OR tocilizumab in first line or after failure with other biotherapy. In case of previous rituximab treatment, inclusion may be possible at least 12 months after the last rituximab infusion or,
• Subcutaneous form of tocilizumab, either as first line or after switch from infusion tocilizumab form is allowed.
- Having given written informed consent prior to undertaking any study-related procedures.
- Covered by a health insurance system where applicable, and/or in compliance with the recommendations of the national laws in force relating to biomedical research.

Exclusion criteria

- Under any administrative or legal supervision.
- Patients having previously received rituximab in the past 12 months.
- Conditions/situations such as:
• Patients with conditions/concomitant diseases making them non evaluable for the primary endpoint
• Requirement for concomitant treatment that could bias primary evaluation
• Impossibility to meet specific protocol requirements (e.g. blood sampling)
• Patient is the Investigator or any sub-investigator, research assistant, pharmacist, study

coordinator, other staff or relative thereof directly involved in the conduct of the protocol
• Uncooperative or any condition that could make the patient potentially non-compliant to the study procedures
- Pregnant or breast-feeding women

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2014
Enrollment:	250
Type:	Actual

Ethics review

Approved WMO Date:	12-12-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL45802.018.13