Experimental protocols for investigating immunogenicity to biopharmaceuticals in patients with immune mediated inflammatory disease (IMIDs)

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Primary objective:- To identify the immunological signature specific of patients who are treated with BP and develop ADA compared to those who do not develop ADA, patients who are BP naive and healthy donors. Secondary objective:- To identify…

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

Summary

ID

NL-OMON45746

Source
ToetsingOnline

Brief title
Cross-sectional ABIRISK project

Condition

- Autoimmune disorders

Synonym
Rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ABIRISK

Intervention

Keyword: Anti-drug antibodies, Biologicals, Rheumatoid arthritis

Outcome measures

Primary outcome

Primary endpoint: activation, maturation and differentiation of biological

specific lymphocytes.ten

Secondary outcome

Secondary parameters/outcomes:

- Ex-vivo evaluation of early biomarkers as potential predictors of

immunogenicity

- Evaluation of AD T cell response

- T- and B-cell AD responses: clonality analysis and epitope mapping

- Evaluation of B cell AD cellular response

- Genetic susceptibility of ADA

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 number of biological/biotechnology-derived proteins used as therapeutic agents (called Biopharmaceuticals) is steadily increasing. Biopharmaceuticals

(BP) may induce an unwanted immune response in treated patients. Immunogenicity related to Biopharmaceuticals (BP) therapy refers to a specific anti-drug antibody (ADA) response. Such immunogenicity may represent a major factor impairing the efficacy of BP due to BP neutralization and also to hypersensitivity reactions that are IgE or non-IgE-mediated. Production of ADA represents the final stage of a complex immune process involving antigen presentation followed by activation of both adaptive and regulatory cellular immune responses. The prediction, prevention and cure of anti-drug (AD) immunization are major goals in BP development. Therefore, in order to minimize the risk of ADA induction and improve sustainable BP efficacy, ABIRISK project is focusing its efforts on understanding mechanisms by which BP drive immune cell activation and ADA production.

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.

Study objective

Primary objective:
- To identify the immunological signature specific of patients who are treated with BP and develop ADA compared to those who do not develop ADA, patients who are BP naive and healthy donors.

Secondary objective:
- To identify molecular, cellular and genetic biomarkers associated with the presence of ADA after three months treatment with BP.
- To identify the specific functional features of immune cells (including T and B lymphocytes, monocyte and dendritic cells) associated with the development of ADA compared to patients that do not develop ADA, BP naive patients and healthy volunteers.
- To identify the genetic signature associated with the development of ADA compared to patients that do not develop ADA, BP naive patients and healthy volunteers.

Study design

Cross-sectional cohort in patients with immune-mediated inflammatory diseases (IMID).
The total duration of study is 1 year, it includes 9 months for inclusion period and 3 months for duration of patient participation

Study duration for each patient:
1. minimum 3 months and maximum 2 years after BP therapy
If ADA+:
2. when ADA status is known (approximately 3 months after the first visit)

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 an IMID
- Patients being treated in the usual manner in accordance with the terms of the marketing authorization and independently from entry into this study:
* Patients treated with Anti TNF therapy for over three months i.e. adalimumab, etanercept or infliximab in first line independently from inclusion into study or,
* Patients treated with Rituximab after failure with anti-TNF therapy or other biotherapy or given in first line or
* Patients treated with Tocilmumab after failure with anti-TNF therapy or other biotherapy or given in first line
- 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.
- Conditions/situations such as:
* Patients with conditions/concomitant diseases making them non evaluable for the primary endpoint
* 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, currently or in the last three months prior to inclusion.
- Patients who have been vaccinated in the last three months prior to inclusion.

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):	06-07-2016
Enrollment:	108
Type:	Actual

Ethics review

Approved WMO

Date:	28-04-2016
Application type:	First submission
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	NL56053.018.15