Efficacy of B cell-targeted therapy in autoimmune bullous diseases

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To characterize the immunological read out, e.g. the immune cell compartments, and antibodies of patients with autoimmune bullous diseases during rituximab treatment and during relapses.

Ethical review	Approved WMO
Status	Pending
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON51059

Source
ToetsingOnline

Brief title
B cell-targeted therapy in AIBD

Condition

- Epidermal and dermal conditions

Synonym
autoimmune bullous diseases, blistering diseases

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: b-cell, pemphigoid, pemphigus vulgaris, rituximab, therapy

Outcome measures

Primary outcome

B-cell phenotype, B-cell repertoire, including number of expanded B-cell clones

Secondary outcome

Laboratory serum and cellular parameters:

• Antigen-specific B cell receptor sequences

• RNA expression profile of antigen-specific B-cells

• Peripheral blood mononuclear cells (PBMC*s)

• Free light chains (FLCs) as a biomarker for plasmacells

• Anti-desmoglein 1 and 3 antibodies

• Antibodies against the noncollagenous 16A domain of BP180 (NC16A) and BP230

• Serum B-lymphocytes, T-lymphocytes

• Serum total IgG and subclasses

• Glycosylation status and binding characteristics of IgG antibodies

Clinical parameters:

• Response outcomes were defined according to international consensus and measured by the early endpoint disease control (DC), and the late endpoints partial remission (PR), complete remission (CR), and the number of relapses.

• Pemphigus Disease Area Index (PDAI)

• Bullous Pemphigoid Disease Area Index (BPDAI)

• Mucous Membrane Pemphigoid Disease Area Index (MMPDAI)

• Adjuvant immunomodulatory or immunosuppressive treatment

• Dermatology Life Quality Index (DLQI)

• Treatment of Autoimmune Bullous Disease Quality of Life (TABQOL)

• Visual Analogue Scale (VAS) pain and itch

• Geriatric 8 (G-8) Score in patients above 50 years

Study description

Background summary

Rituximab is a chimeric murine-human monoclonal antibody that binds and targets the CD20 antigen of B-lymphocytes. It is used to eliminate B-cell immunoreactivity in autoimmune bullous diseases, including pemphigus diseases, bullous pemphigoid and mucous membrane pemphigoid. Recently rituximab is approved for pemphigus vulgaris. Understanding the mechanisms of action of B-cell targeted therapy is essential to optimize tailored therapeutic strategies and to get more knowledge about the predictive factors for disease relapses during and after treatment. The aim of this study is to prospectively collect multi-layered standardized clinical data, patient-reported outcome measures (PROMS) and biosamples in patients with autoimmune bullous diseases to allow for standardized comparison of the immunological processes during different phases of disease activity.

Study objective

To characterize the immunological read out, e.g. the immune cell compartments, and antibodies of patients with autoimmune bullous diseases during rituximab treatment and during relapses.

Study design

Explorative, prospective observational cohort study.

Study burden and risks

Participation in this study has negligible risk because the only intervention done is venapuncture to obtain blood. In principal, study visits will be planned to coincide with standard clinical visits to decrease the burden for

participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age of 18 years or older.
• Diagnosis of pemphigus, based on the following criteria: clinical features suggestive of pemphigus vulgaris or pemphigus foliaceus; a histological image of intraepidermal acantholysis; and/or deposition of IgG, complement component 3, or both on the keratinocyte membrane detected by direct immunofluorescence
• Diagnosis of pemphigoid, based on the following criteria: linear depositions of IgG, IgA, IgM, or C3c along the BMZ by direct immunofluorescence microscopy (DIF) and/or positive indirect immunofluorescence microscopy (IIF) on salt-split skin (SSS), in combination with clinical presentation, histopathological findings, or other immunoserological tests compatible with

the diagnosis of a pemphigoid disease.
• Administration of rituximab according to the following protocol: two infusion of 1000mg within an interval of two weeks, followed by 500mg at month 6 and month 12, or in patients with severe pemphigus 1000mg at month 6, or in patients who are not in complete remission two infusions of 1000mg two weeks apart.

Exclusion criteria

• Patients under the age of 18 years.
• Plasma exchange, plasmapheresis or immunoadsorption within the last 3 months

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2022
Enrollment:	200
Type:	Anticipated

Ethics review

Approved WMO

Date:	17-11-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL76959.042.21