# Short-term safety, efficacy and mode of action of apremilast in mild to moderate cutaneous pemphigoid: a phase IIa open label single arm study.

Published: 09-04-2019
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Primary Objective: To evaluate the achievement of partial remission by apremilast combined with doxycyclineat week sixteen (t=16). Secondary Objectives: • Complete remission at week sixteen; • Disease control at week six (t=6); • Drug survival;•...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Epidermal and dermal conditions |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON49116

**Source**
ToetsingOnline

**Brief title**
SAMP trial

### Condition

- Epidermal and dermal conditions

**Synonym**
parapemphigus

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Groningen

**Source(s) of monetary or material Support:** Ministerie van OC&W,Amgen

## Intervention

**Keyword:** apremilast, investigator initiated study, PDE4, pemphigoid

## Outcome measures

### Primary outcome

Partial remission will be analysed in week sixteen (t=16). Partial remission is defined as presence of transient new lesions that heal within one week OR >=30% decrease of VAS. At week six (t= 6), patients that showed no disease control on apremilast combined with doxycycline will be excluded from the pilot study. Disease control is defined as *the time that new lesions cease to form and established lesions begin to heal OR pruritic symptoms start to abate (minimal 1-point decrease of VAS)*.

### Secondary outcome

• Achievement of complete remission at week sixteen. Complete remission is defined as absence of new or established lesions or pruritus.30

• Proportion of patient with drug survival at t=16.

• Proportion of patients with disease control at t=6.

• Mean decrease in periphery blood eosinophil count.

• Mean decrease in BP180 Nc16a titers by ELISA.

• Change in genexpression by RNA sequencing measured at t=0 and t=16.

The following outcomes will be used for measuring clinical efficacy:

• mean reduction in Visual Analogue Scale (VAS)

• mean decrease in Dermatology Quality of Life index (DLQI), autoimmune

blistering disease quality of life (AIBDQOL) and treatment autoimmune bullous

diseases quality of life (TABQOL);

• mean reduction of Bullous Pemphigoid Disease Area Index (BPDAI).

# Study description

### Background summary

Pemphigoid is the most common chronic autoimmune disease of the skin and mucosae. It is characterized by subepidermal blistering caused by autoantibodies directed against hemidesmosomal proteins BP180 and BP230 located in the basement membrane zone.
Pemphigoid is often treated with systemic corticosteroids. In the absence of treatment, pemphigoid has a tendency to relapse. Systemic corticosteroids however, are associated with serious adverse effects, morbidity and mortality. Therefore, there is a need for safer treatment options. In this pilot efficacy study the treatment response of apremilast combined with doxycycline in mild to moderate cutaneous pemphigoid will be evaluated. We hypothesize an impairment of immune-complex-induced neutrophil activation caused by PDE4 inhibition, making it a potential target for the treatment of pemphigoid diseases. This is based on the facts that PDE4 is the key enzyme accounting for cAMP degradation in neutrophils and PDE4 inhibitors are highly effective to curb neutrophil functions. An animal study showed reduction in blistering by PDE4 inhibitors in antibody transfer-induced epidermolysis bullosa acquisita and also hindered disease progression in immunization-induced epidermolysis bullosa acquisita.

### Study objective

Primary Objective:
To evaluate the achievement of partial remission by apremilast combined with doxycycline
at week sixteen (t=16).

Secondary Objectives:
• Complete remission at week sixteen;
• Disease control at week six (t=6);
• Drug survival;
• Clinical efficacy;
• Mean decrease in periphery blood eosinophil count;
• Mean decrease in BP180 Nc16a titers by ELISA;
• Change in genexpression by RNA sequencing measured at t=0 and t=16.

### Study design

This is an open label, single arm study in 10 patients with pemphigoid.

### Intervention

Investigational product: apremilast (Otezla)
Non-investigational product: doxycycline

Included subject will be treated with doxycycline during 6 weeks and apremilast during 16 weeks.

### Study burden and risks

Eligble patients will be recruited during routine clinical care. There is a total of 7 visits. The patients will undergo a screening which forms part of the inclusion phase. All patients will be screened for hepatitis B and C, HIV and tuberculosis (TBC) by blood test. Moreover, an X ray will be performed for TBC screening before starting therapy. Fertile female participants will undergo a serum pregnancy test. At screening, patients will have their medical history taken and will undergo a physical exam by a physician including measuring vital signs (blood pressure, heart rate, temperature). This will be taken every visit including VAS, BPDAI score and checking for adverse events. Moreover, photodocumentation will be taken at every visit. Laboratory tests will be taken at baseline, week 6 and week 16, and if necessary on indication during other visits. At baseline and week 16 two perilesional punch biopsy will be taken.

## 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

adult (>= 18 years of age) male or female patients with recently diagnosed mild to moderate localized or generalized cutaneous pemphigoid, or patients that were in complete remission without treatment that have a mild to moderate flare-up of the disease.

## Exclusion criteria

Women of childbearing potential without contraception; women who are pregnant or planning to become pregnant or who are lactating; patients that use systemic immunosuppressive medication provided the treatment cannot be stopped before Visit 2; any condition which would make the patient unsuitable for treatment, or requires steroid use. Patients with PHQ-9 (Patients Health Questionnaire-9) score >= 10. Contradiction or known allergy for PDE4 inhibitors;

# Study design

## Design

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|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |

| | |
|---|---|
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 10-07-2019 |
| Enrollment: | 10 |
| Type: | Actual |

### Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Doxycycline |
| Generic name: | Doxycycline |
| Registration: | Yes - NL outside intended use |
| Product type: | Medicine |
| Brand name: | Otezla |
| Generic name: | Apremilast |
| Registration: | Yes - NL outside intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 09-04-2019 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 23-04-2019 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 20-06-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 22-07-2019 |

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| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 26-08-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 09-09-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 30-10-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 25-11-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 04-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 07-07-2020 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 29-07-2020 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 24-09-2020 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 07-06-2021 |

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|---|---|
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 24-06-2021 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 02-08-2021 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 10-09-2021 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 06-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 22-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 02-11-2022 |
| Application type: | Amendment |
| 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 |
|---|---|
| EudraCT | EUCTR2018-002564-10-NL |
| CCMO | NL66819.042.18 |