A Phase 2, randomized, double-blind, placebo-controlled, multicenter proof-of-concept study evaluating efficacy and safety of rilzabrutinib (SAR444671) in adult patients with moderate-to-severe atopic dermatitis who are inadequate responders or intolerant to topical corticosteroids

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Primary objective:Assess the efficacy of rilzabrutinib in participants with atopic dermatitis (AD)Secondary objectives: * Assess the efficacy of rilzabrutinib at different time points* Assess the safety of rilzabrutinib

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

Summary

ID

NL-OMON52158

Source
ToetsingOnline

Brief title
ACT17207

Condition

- Autoimmune disorders
- Epidermal and dermal conditions

Synonym
Atopic Dermatitis ; Atopic Eczema

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Atopic Dermatitis, eczema, phase 2, Rilzabrutinib

Outcome measures

Primary outcome

Primary endpoint:

- Percent change in Eczema Area and Severity Index (EASI) score from baseline

to week 16

Secondary outcome

Secundary endpoints:

- Proportion of participants with Investigator's Global Assessment (IGA) of 0

or 1 (disease

free or almost disease free) compared to placebo at week 16

- Proportion of participants achieving EASI-75 at week 16

- Proportion of participants with reduction of weekly average of daily peak

pruritus Numerical

Rating Scale (PP-NRS) of *4 points from baseline to week 16

- Time to onset of effect on pruritus until week 16

- Absolute change in EASI score from baseline to week 16

- Proportion of participants achieving EASI-50/90 at week 16

- Change in percent body surface area (BSA) of from baseline to week 16

EASI

- Change on weekly average of daily PP-NRS from baseline to week 16

- Incidence of treatment-emergent adverse events (TEAEs), serious adverse events

(SAEs), and adverse events of special interest (AESIs) up to week 17

- Incidence of study investigational medicinal product (IMP) discontinuation

and withdrawals

due to TEAEs from baseline to week 16

Study description

Background summary

Rilzabrutinib (also known as SAR444671 or PRN1008), a selective Bruton*s tyrosine kinase
(BTK) inhibitor, is an investigational drug being developed as an oral agent for the treatment of
immune-mediated dermatological diseases. This study will explore the efficacy and safety of
rilzabrutinib in participants with moderate to severe atopic dermatitis (AD).

Study objective

Primary objective:
Assess the efficacy of rilzabrutinib in participants with atopic dermatitis (AD)

Secondary objectives:
* Assess the efficacy of rilzabrutinib at different time points
* Assess the safety of rilzabrutinib

Study design

This is a parallel, treatment, Phase 2, double-blind, 2-arm, placebo-controlled

study to evaluate
the efficacy and safety of rilzabrutinib in adult participants (aged at least 18 years) with moderate to-severe AD and intolerance or inadequate response to topical corticosteroids (TCS).
An optional substudy will be proposed to participants for skin tape strip samples to be taken at
baseline and Week 16 for exploratory biomarkers analysis.

Intervention

The total study duration per participant is expected to be approximately 21 weeks, including:
* Screening: up to 4 weeks
* Double-blind investigational medicinal product (IMP) treatment period: 16 weeks ± 3 days
* Post-treatment follow-up: 1 week ± 3 days.
Study intervention(s)
Investigational medicinal products: Rilzabrutinib and placebo
Rilzabrutinib (SAR444671)
* Formulation: tablets (modified-capsule shaped tablets / caplets)
* Route of administration: oral
* Dose regimen: 400 mg twice daily (BID) (morning and evening) or 400mg three times daily (TID) (morning, afternoon and evening).
Placebo
* Formulation: tablets (modified-capsule shaped tablets / caplets) (identical in appearance
and contain the same inactive ingredients as that of the rilzabrutinib formulation, but do
not contain rilzabrutinib)
* Route of administration: oral
* Dose regimen: BID (morning and evening) or TID (morning, afternoon and evening)
Rilzabrutinib or placebo may be taken with or without food (gastrointestinal tolerability may be
better if given with food).

Study burden and risks

Risks related to blood draws and side effects of the study drug.

Contacts

Public

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Atopic Dermatitis (AD) as defined by the American Academy of Dermatology Consensus Criteria.
- History of AD for at least 12 months prior to baseline as determined by the Investigator through patient interview.
- Eczema Area and Severity Index (EASI) score * 12 at screening and * 16 at baseline.
- IGA score * 3 (on the 0 to 4 IGA scale) at baseline.
- BSA of AD involvement * 10% at baseline.
- Documented inadequate response or intolerance to TCS within 6 months prior to baseline visit
- Baseline PP-NRS score for maximum itch intensity *4.
- All contraceptive use by men and women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
- For optional substudy only: Willingness to have 2 tape strips for comparison of

baseline and treatment response.

Exclusion criteria

- Skin comorbidities that may interfere with study assessments such as psoriasis,
tinea corporis, lupus erythematosus.
- Conditions that may predispose the patient to excessive bleeding.
- Any other clinically significant disease, condition or medical history that, in the
opinion of the Investigator, would interfere with participant safety, trial evaluations, and/or trial procedures.
- Laboratory abnormalities at the screening visit
- History of serious infections requiring intravenous therapy with the potential for
recurrence (as judged by the Site Investigator and the Sponsor Medical Monitor), with less than 4 weeks interval between resolution of serious infection and first dose of study drug, or currently active moderate to severe infection at Screening (Grade
2 or higher) including active coronavirus disease 2019 (COVID-19).
- Live vaccine except Bacille Calmette Guerin-vaccination within 28 days prior to
Day 1 or plan to receive one during the trial; Bacille Calmette Guerin-vaccination
within 12 months prior to Screening.
- COVID-19 vaccine within 14 days prior to Study Day 1.
- Refractory nausea and vomiting, malabsorption, external biliary shunt, or significant bowel resection that would preclude adequate rilzabrutinib/placebo absorption.
- Initiation of prescription moisturizers (with or without additives such as ceramide, hyaluronic acid, urea, or filaggrin), topical anesthetics or antihistamines during the screening period.
- Use of TCS, topical calcineurin (tacrolimus, and/or pimecrolimus) or topical phosphodiesterase 4 inhibitor within 1 week prior to baseline and as concomitant medication.
- Use of systemic corticosteroids within 4 weeks prior to baseline and as concomitant medication.
- Phototherapy for AD or regular use (more than 2 visits per week) of a tanning booth/parlor within 4 weeks prior to baseline or likely to be required as concomitant procedure during the study.
- Use of mycophenolate mofetil, azathioprine, methotrexate, cyclosporine, dapsone, intravenous immunoglobulin (IVIG), Kineret (anakinra), Enbrel (etanercept), or any other immunosuppressant not mentioned in this exclusion criterion within 4 weeks prior to baseline.
- Use of infliximab, adalimumab, golimumab, abatacept, tocilizumab,

certolizumab, secukinumab, IFN-*, JAK inhibitors, dupilumab, and any other biologic or targeted-synthetic disease modifier drug not mentioned in this exclusion criterion or in exclusion criterion above, as well as plasmapheresis within 12
weeks prior to baseline.
- Use of anti-CD20 drugs such as rituximab, ofatumumab, other long-acting biologics within 6 months prior to baseline (or shorter if there is documented B
cell reconstitution for anti-CD20 drugs).
- Use of proton pump inhibitor drugs such as omeprazole and esomeprazole within 3 days of baseline (it is acceptable to change participant to H2 receptor
blocking drugs prior to baseline).
- Concomitant use of known strong-to-moderate inhibitors and inducers of cytochrome P450 3A (CYP3A) within 14 days or 5 half-lives (whichever is longer) prior to baseline.
- Previous use of a BTK inhibitor.
- Has received any investigational drug (or is currently using an investigational
device) within the 30 days before baseline, or at least 5 times the respective elimination half-life time (whichever is longer).
- Active TB or a history of incompletely treated TB, Quantiferon positive patients,
Clinically significant abnormality consistent with prior/active TB infection based
upon chest radiograph with at least posterior-anterior view, Suspected extrapulmonary TB infection, or patients at high risk of contracting TB

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2022
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	Rilzabrutinib

Ethics review

Approved WMO Date:	24-08-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-10-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	11-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2021-001704-15-NL
CCMO	NL78166.041.21