Randomized, double blind, multicenter extension to CZPL389A2203 dose-ranging study to assess the shortterm and long-term safety and efficacy of oral ZPL389 with concomitant or intermittent use of TCS and/or TCI in adult patients with atopic dermatitis (ZEST Extension)

Published: 20-05-2019
Last updated: 09-04-2024

The purpose of this study is to assess short-term and the long-term safety and efficacy of oral ZPL389 (30 mg once daily (o.d.) and 50 mg o.d.) when used concomitantly or intermittently with topical corticosteroid (TCS) and/or topical calcineurin…

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

Summary

ID

NL-OMON49671

Source
ToetsingOnline

Brief title
CZPL389A2203E1 (ZEST Extension)

Condition

- Epidermal and dermal conditions

Synonym
atopic eczema, Neurodermitis

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Atopic dermatitis, Chronic inflammatory skin disease, H4R antagonist, ZPL389

Outcome measures

Primary outcome

To assess the short-term and long-term safety of 30 mg o.d. and 50 mg o.d.

ZPL389 with concomitant or intermittent use of TCS and/or TCI up to total of 32

weeks and 116 weeks of treatment.

Secondary outcome

* To evaluate the efficacy of 30 mg o.d. and 50 mg o.d. ZPL389 with concomitant

or intermittent use of TCS and/or TCI as assessed by investigator's global

assessment (IGA) response over time.

* To evaluate the efficacy of 30 mg o.d. and 50 mg o.d. ZPL389 with concomitant

or intermittent use of TCS and/or TCI as assessed by eczema area and severity

index (EASI) over time.

Study description

Background summary

Atopic dermatitis is also called atopic eczema. It is a form of skin inflammation. Symptoms include itching, redness and swelling of the skin. The skin spots can be moist and may have scabs on it. Two to ten percent of the

adults and up to 20 percent of the children have AD, of which about 70% and 16% are moderate to severe. The usual treatment of AD consists of moisturizing cream, anti-inflammatory ointment (eg with corticosteroids), light therapy and anti-inflammatory pills ". Unfortunately, some of the patients have insufficient benefit from these existing treatments or can not tolerate them well. There is therefore a need for new medicines.

ZPL389 is a substance that attaches to a body protein called the histamine 4 receptor (H4R). Histamine is made by the body when it comes into contact with a substance for which it is hypersensitive. Histamine attaches itself to the H4R and therefore causes skin symptoms such as itching. ZPL389 is so firmly attached to the H4R that histamine can no longer attach itself to it. We therefore expect that ZPL389 can counteract the symptoms of atopic dermatitis.

Study objective

The purpose of this study is to assess short-term and the long-term safety and efficacy of oral ZPL389 (30 mg once daily (o.d.) and 50 mg o.d.) when used concomitantly or intermittently with topical corticosteroid (TCS) and/or topical calcineurin inhibitors (TCI) (according to a standardized regimen, depending on atopic dermatitis lesion severity, in line with common/ real world practice) for up to approximately 2 years in adult patients with atopic dermatitis who previously completed 16 weeks of treatment in the core study (CZPL389A2203).

Study design

This 2-year study is a randomized, double blind, parallel group, 2-arm study in up to approximately 202 to 230 subjects with atopic dermatitis (AD) who have completed 16 weeks of treatment in the CZPL389A2203 (core study). In this extension study, subjects who have been receiving ZPL389 30 mg o.d. or 50 mg o.d. doses in the core study, will continue to receive the same doses. Subjects who were receiving ZPL389 3 mg, 10 mg or placebo in the core study will be randomized into 30 mg o.d. or 50 mg o.d. ZPL389 in a 1:1 ratio. All subjects will receive concomitant or intermittent TCS and/or TCI along with ZPL389. Subjects, after completing 100 weeks of treatment during extension study (i.e. up to Week 116 starting from Week 16 of the core study), will enter a treatment-free follow-up period for 4 weeks.

Intervention

ZPL389 will be administered orally in capsules in one of the two following treatment arms:
ZPL389 30 mg o.d. + TCS and/or TCI
ZPL389 50 mg o.d. + TCS and/or TCI

Study burden and risks

During the total course of the trial the following assessments will be done/requested:
- Physical examination: 12x
- ECG: 12x
- Vital signs: 12x
- Blood test (10 ml): 12x
- Pregnancy test (if applicable) 12x
- Urine test: 13x
- Diary completion: daily
- Complete questionnaires: 6x

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Signed informed consent must be obtained before any assessment is performed.
* Female and male subjects with atopic dermatitis who have participated in and completed 16 weeks of study treatment in CZPL389A2203 study.
* Willing and able to comply with scheduled visits, treatment plan, laboratory tests, diary
completion and other study procedures.

Exclusion criteria

* Inability to use TCS and/or TCI concomitantly or intermittently due to history of important side effects of topical medication (e.g. intolerance to treatment, hypersensitivity reactions, significant skin atrophy, systemic effects), as assessed by the investigator or subject*s treating physician.
* Subjects who met any study and/or treatment discontinuation criteria during the
CZPL389A2203 study.
* Any active skin disease that, in the opinion of the investigator, would confound the diagnosis
or evaluation of AD disease activity (e.g. Netherton Syndrome, Cutaneous T-Cell Lymphoma, extensive contact dermatitis, chronic actinic dermatitis).
* Subjects taking medications prohibited by the protocol.
* Pregnant or nursing (lactating) women.
* Women of child-bearing potential (WOCBP), defined as all women physiologically capable of becoming pregnant, unless they use required methods of contraception during dosing and for 4 weeks after stopping of investigational medication.
* Sexually active males unless they use a condom during intercourse while taking drug and for 4 weeks after stopping investigational medication and should not father a child in this period. A condom is required to be used also by vasectomized men in order to prevent delivery of the drug via seminal fluid.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	18-02-2020
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	ZPL389
Generic name:	adriforant

Ethics review

Approved WMO Date:	20-05-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-02-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	24-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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□000595□15-NL
ClinicalTrials.gov	NCT03948334
CCMO	NL69078.078.19