A phase 3 multicenter, long-term extension study investigating the efficacy and safety of abrocitinib, with or without topical medications, administered to subjects aged 12 years and older with moderate to severe atopic dermatitis

Published: 20-08-2018
Last updated: 12-04-2024

Primary Objective• To estimate the long term safety of 100 mg and 200 mg once daily (QD) of abrocitinib with or without topical treatments in adult and adolescent subjects who previously participated in qualifying abrocitinib atopic dermatitis (AD)…

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

Summary

ID

NL-OMON54631

Source
ToetsingOnline

Brief title
B7451015 (9002/0535)

Condition

- Epidermal and dermal conditions

Synonym
Atopic dermatitis, atopic eczema

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: The sponsor as described in question B6/B7

Intervention

Keyword: Abrocitinib (PF-04965842), Atopic dermatitis, Phase 3

Outcome measures

Primary outcome

Primary endpoints

• The incidence of treatment emergent adverse events.

• The incidence of serious adverse events and adverse events leading to discontinuation.

• The incidence of clinical abnormalities and change from baseline in clinical laboratory values, ECG measurements, and vital signs.

Secondary outcome

Secondary endpoints

Baseline, for efficacy endpoints, is defined as pre dose Day 1 in the relevant qualifying parent study.

• Response based on achieving the Investigator*s Global Assessment (IGA) score of clear (0) or almost clear (1) (on a 5 point scale) and a reduction from baseline of >=2 points at all scheduled time points.

• Response based on achieving >=50%, >=75%, >=90% and 100% improvement from baseline in the Eczema Area and Severity Index (EASI) total score (EASI50, EASI75, EASI90 and EASI100) at all scheduled time points.

• Response based on achieving an improvement >=4 points from baseline in the severity of pruritus numerical rating scale (NRS) at all scheduled time points.

• Change from baseline in the frequency of itching due to Atopic Dermatitis

• Change from baseline of Patient Global Assessment (PtGA) at all scheduled time points.

• Change from baseline in the percentage Body Surface Area (BSA) affected at all scheduled time points.

• Change from baseline in Dermatology Life Quality Index (DLQI) or Children*s DLQI (CDLQI) at all scheduled time points.

• Change from baseline in Patient Oriented Eczema Measure (POEM) at all scheduled time points.

• Change from baseline in Hospital Anxiety and Depression Scale (HADS) at all scheduled time points.

• Change from baseline in European Quality of Life 5 Dimension 5 Level Scale (EQ 5D 5L) or European Quality of Life 5 Dimension Youth Scale (EQ 5D Y) at all scheduled time points.

• Steroid-free Days at all scheduled time points.

• Serum hsCRP levels at all scheduled time points.

Study description

Background summary

Atopic dermatitis, also known as atopic eczema, is a common, chronic, inflammatory skin disorder characterized by flaky skin lesions, intense pruritus, and a general deterioration in the quality of life. Over the past 50 years, AD has become more prevalent, especially in industrialized, temperate

countries such as the US. AD is one of the most common, chronic, relapsing childhood dermatoses, impacting 15 30% of all children in the US and many have disease that persists into adulthood with a lifetime prevalence of those affected in childhood reported to be 34%

There are a limited number of treatments available for AD and those that are available have multiple limitations. The topical therapies have drawbacks related to the duration of use due to the potential for local and systemic side effects and to the body regions of use. For AD patients not responding to topical therapies and phototherapy, off label use of systemic agents, which include oral corticosteroids or oral immunosuppressants, remain the last viable treatment option. Systemic therapy options are associated with potentially severe adverse effects and require careful monitoring. The risk of toxicity and side effects remain a concern when systemic agents are used. For these reasons the use of these agents is limited to short courses or intermittent therapy.

Therefore, the predominant unmet medical need is for a conveniently administrered therapy with an acceptable safety profile for long term continuous and intermittent use which is effective for moderate to severe AD not controlled with topical therapies. Abrocitinib is provided as an orally administered tablet, which is a more convenient treatment for patients with moderate to severe AD.

Abrocitinib is an orally bioavailable small molecule that selectively inhibits JAK1 by blocking the ATP binding site. A variety of pro inflammatory cytokines such as IL 4, IL 13, IL 22, IL 31 and IFN-gamma , have been suggested to have a role in the pathogenesis of AD. Many of these pathogenic cytokines use the JAK1 for signaling. Therefore, JAK1 is an attractive therapeutic target for AD as an innovative oral therapeutic agent.

Study objective

Primary Objective
• To estimate the long term safety of 100 mg and 200 mg once daily (QD) of abrocitinib with or without topical treatments in adult and adolescent subjects who previously participated in qualifying abrocitinib atopic dermatitis (AD) Phase 3 trials.

Secondary Objectives
• To estimate the long term efficacy of abrocitinib.

Study design

This is a multicenter, long-term extension study to evaluate the long term safety and efficacy of abrocitinib administered to subjects aged 12 years and

older with moderate to severe AD. Subjects must have completed a qualifying parent study and remain eligible to receive abrocitinib, or have completed the full rescue treatment/open-label run-in period of B7451014 and failed to meet the protocol defined response criteria at week 12. Based on treatment assignment, abrocitinib will be administered orally at doses of 200 mg or 100 mg once daily (QD). The maximum total treatment duration for individual subjects may differ, as this will be variable; The duration of the study for adults who remain eligible and active in the study will be until at least 2024; The duration of the study for adolescents who remain eligible and active in the study will be until they reach 18 years of age, or until 2024, whichever is later. After these time points, as relevant, a subject may continue to receive Investigational
Product in this LTE) study at the discretion of the sponsor regardless of availability of commercial product in their country, or until the sponsor terminates the study in that country (see Section 14). Subjects will enter a 4 week follow up period after permanent discontinuation of treatment. Medicated and non-medicated topical treatments for AD are permitted throughout the study. Systemic treatments for AD are prohibited throughout the study. Concomitant medication for adverse events or other non AD concomitant medical conditions are permitted throughout the study, unless listed as a prohibited medication (Appendix 18, Appendix 19).

Subjects who meet eligibility criteria for this long term extension study will undergo screening/baseline/Day -1 assessments (as required per the Schedule of Activities). Subjects previously randomized to either dose of active investigational product, either abrocitinib 200 mg or 100 mg QD in the qualifying parent study will be allocated to the same dose in this long-term extension study, and the blind will be maintained throughout Treatment Period 1. Subjects previously randomized to active control drug or placebo only in a qualifying parent study will be randomized to double-blind treatment in this long-term extension study during Treatment Period 1; either abrocitinib 200 mg or 100 mg QD. For exceptions please see the protocol.

Open-label drug will be provided to all subjects in Treatment Period 2, in line with their previously allocated dose.

Intervention

All subjects receive either 100 or 200 mg abrocitinib daily.

Study burden and risks

Please refer to appendix D of the subject information sheet for an overview of the side effects and possible risks of the study.

Contacts

Public
Pfizer

Hudson Boulevard East 66
New York 10001
US
Scientific
Pfizer

Hudson Boulevard East 66
New York 10001
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Evidence of a personally signed and dated informed consent document indicating that the subject or their parent(s)/legal guardian, if applicable, have been informed of all pertinent aspects of the study.
2. Male or female subjects of 12 years of age or older, at the time of informed consent and meets inclusion criterion for minimum body weight (if applicable) from qualifying parent study. Adolescent subjects below the age of 18 years old (or country-specific age of majority) will only be enrolled in this study if instructed by the sponsor and approved by the country or regulatory/health authority. If these approvals have not been granted, only subjects aged 18 years (or country-specific age of majority) and older will be enrolled.

3. Willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures.
4. Must have completed the full treatment period of a qualifying parent study OR must have completed the full rescue treatment period of a qualifying parent study (if applicable). OR must have completed the full open-label run-in period in B7451014 and did not meet the protocol-specified response criteria at week 12.
5. Female subjects who are of childbearing potential (which includes all female subjects aged 12 years and older, regardless of whether they have experienced menarche) must not be intending to become pregnant, currently pregnant, or lactating. The following conditions apply:
a. Female subjects of childbearing potential must have a confirmed negative pregnancy test prior to allocation to treatment.
b. Female subjects of childbearing potential must agree to use a highly effective method of contraception (as per Section 4.4.1) for the duration of the active treatment period and for at least 28 days after the last dose of investigational product.
For Czech Republic only, 5 b. is revised and 5 c. is added to require:
Female subjects of childbearing potential >=15 years of age who are at risk of pregnancy must agree to use a highly effective method of contraception for the duration of the active treatment period and for at least 28 days after the last dose of investigational product;
c. Female subjects less than 15 years of age must not be sexually active, and abstinence per the below definition should be confirmed prior to enrollment.
NOTE: Sexual abstinence, defined as completely and persistently refraining from all heterosexual intercourse (including during the entire period of risk associated with the study treatments) may obviate the need for contraception ONLY if this is the preferred and usual lifestyle of the subject.
6. Female subjects of non-childbearing potential must meet at least 1 of the following criteria:
a. Have undergone a documented hysterectomy and/or bilateral oophorectomy;
b. Have medically confirmed ovarian failure; or
c. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause and have a serum follicle-stimulating hormone (FSH) level confirming the postmenopausal state.
All other female subjects (including female subjects with tubal ligations) are considered to be of childbearing potential.
7. Must agree to avoid prolonged exposure to the sun and not to use tanning booths, sun lamps or other ultraviolet light sources during the study.
8. Must agree to avoid use of prohibited medications throughout the duration of the study, as detailed in Appendix 18 and Appendix 19.

Exclusion criteria

1. Other acute or chronic medical or psychiatric condition including recent (within the past year) or active suicidal ideation or behavior or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.
2. Currently have active forms of other inflammatory skin diseases, ie, not AD or have evidence of skin conditions (eg, psoriasis, seborrheic dermatitis, lupus) at the time of Day -1 that would interfere with evaluation of atopic dermatitis or response to treatment.
3. Discontinued from treatment (or rescue treatment period/open-label run-in period, if applicable) early in a qualifying parent study OR triggered a discontinuation criterion at any point during the qualifying parent study OR meets exclusion criteria from qualifying parent studies which in the opinion of the investigator, or sponsor, is an ongoing safety concern.
4. Ongoing adverse event in the qualifying parent study which in the opinion of the investigator, or sponsor, is an ongoing safety concern.
5. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the investigator, or subjects who are Pfizer employees, including their family members, directly involved in the conduct of the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2019
Enrollment:	20

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Abrocitinib
Generic name:	n/a

Ethics review

Approved WMO Date:	20-08-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-05-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-10-2019
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-02-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-06-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	09-07-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-07-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-04-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	30-06-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-12-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-12-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-11-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2017-004851-22-NL
CCMO	NL66738.100.18