A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Apremilast (CC-10004) in Pediatric Subjects from 6 through 17 Years of Age with Moderate to Severe Plaque Psoriasis

Published: 15-01-2019
Last updated: 10-01-2025

Primary ObjectiveThe primary objective of the study is to evaluate the clinical efficacy of apremilastcompared with placebo in children and adolescents (ages 6 through 17 years) withmoderate to severe plaque psoriasis.Secondary Objectives- * To...

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

Summary

ID

NL-OMON55888

Source
ToetsingOnline

Brief title
SPROUT

Condition

- Autoimmune disorders

Synonym
Psoriasis, scaly skin rash

Research involving

Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Biotechnologische Industrie

Intervention

Keyword: Apremilast, Pediatric, Plaque Psoriasis

Outcome measures

Primary outcome

The primary endpoint is the proportions of subjects achieving sPGA response at Week 16 (defined as sPGA score of clear (0) or almost clear (1) with at least a 2-point reduction from baseline at Week 16).

Secondary outcome

Major Secondary Endpoint: Proportion of subjects who - in week 16 - achieve at least a 75% reduction in PASI (PASI-75) from baseline.

Other Secondary Endpoints are:

-Proportion of subjects who - at week 16 - achieve at least a 50% reduction in PASI (PASI-50) from baseline

- Percent change from baseline in total PASI score at week 16

- Percent change from baseline in affected BSA at week 16

- Proportion of subjects who achieve CDLQI (0/1) at week 16

- Change from baseline in CDLQI score at week 16

Study description

Background summary

The treatment options for pediatric patients with plaque psoriasis, including approved systemic medications, remain limited. Moreover, fear of needles is common in children. Thus, there remains an unmet need for effective systemic therapies that offer oral convenient dosing and a favorable benefit/risk profile for the treatment of pediatric patients with moderate to severe plaque psoriasis.

Apremilast is an oral selective phosphodiesterase type 4 (PDE4) inhibitor marketed worldwide under the trade name Otezla. Apremilast 30 mg twice per day (BID) received its first global marketing approval for the treatment of adult patients with moderate to severe plaque psoriasis in 2014.

Clinical data from multiple Phase 2 and Phase 3 trials and in the post-marketing setting have demonstrated that apremilast is an effective oral therapy with an acceptable safety profile in adult patients.

Exploratory analyses from a recent Phase 2 study (CC-10004-PPSO-001) indicate that apremilast may be effective for the treatment of moderate to severe plaque psoriasis in the pediatric population as in adults. This Phase 3 study (CC-10004-PPSO-003) is being conducted to evaluate the safety and efficacy of apremilast in the treatment of pediatric subjects, ages 6 through 17 years, with moderate to severe plaque psoriasis.

Study objective

Primary Objective
The primary objective of the study is to evaluate the clinical efficacy of apremilast compared with placebo in children and adolescents (ages 6 through 17 years) with moderate to severe plaque psoriasis.

Secondary Objectives
- * To evaluate the safety and tolerability of apremilast compared with placebo, in children and adolescents (ages 6 through 17 years) with moderate to severe plaque psoriasis
- * To evaluate the effect of apremilast compared with placebo on health-related quality of life (HRQoL).

Study design

This is a multicenter, randomized, double-blind, placebo-controlled efficacy and safety study.
At least 230 pediatric subjects (ages from 6 through 17 years) will be randomized 2:1 to receive either apremilast or placebo for the first 16 weeks. Randomization to the apremilast arm or the placebo arm will be stratified by baseline age group (6 to 11 years or 12 to 17 years). A minimum of 75 subjects will be randomized in each age group. The sponsor may halt enrollment of one age group if that age group reaches 155 randomized subjects to allow the other group to randomize at least 75 subjects. Treatment will be assigned by weight with subjects 20 kg to < 50 kg receiving apremilast 20 mg BID or placebo BID and subjects >= 50 kg receiving apremilast 30 mg BID or placebo BID. After all subjects have completed Week 16 (Visit 7), or discontinued from the study, a Week 16 database lock will be performed; the primary data analysis will be conducted and a Week 16 clinical study report will be generated. Study investigators and subjects will remain blinded to initial treatment assignments until the final database lock at the conclusion of the study. The blind also should be maintained for persons responsible for the ongoing conduct of the study. At the end of the study, after all subjects have either completed Week 52 (Visit 16) and entered the Long-term Study, or completed the Observational Follow-up Phase, or been discontinued from the Apremilast Extension Phase (Weeks 16 to 52) or the Observational Follow-up Phase, a final analysis will be performed and a final clinical study report will be generated.

The study will consist of four phases:
- Screening Phase - up to 35 days
- Placebo-controlled Treatment Phase - Weeks 0 to16
Subjects will be randomly assigned in a 2:1 ratio to weight-based apremilast or placebo. Subjects 20 kg to < 50 kg will receive apremilast 20 mg BID or placebo BID and subjects >= 50 kg will receive apremilast 30 mg BID or placebo BID. The primary endpoint will be the proportion of subjects with a Static Physician Global Assessment (sPGA) score of clear (0) or almost clear (1) with at least a 2-point reduction from baseline at Week 16.
From Week 8 through Week 16, any subject with a Psoriasis Area Severity Index (PASI) increase >= 50% from baseline will be eligible to commence treatment with moderate-to-high potency topical steroid preparations (early escape) and continue with randomized investigational product (IP).
- Apremilast Extension Phase - Weeks 16 to 52
Placebo subjects will be switched at Week 16 to receive apremilast 20 mg BID or 30 mg BID, according to baseline weight. All other subjects will continue to receive either apremilast 20 mg BID or apremilast 30 mg BID based on their original dosing assignment.
- Observational Follow-up Phase - 14 weeks
All eligible subjects who complete the Apremilast Extension Phase may opt to enroll in a separate Long-term Study (for up to 4 years or until approval,

whichever comes first). Subjects who choose not to participate in the Long-term Study, or discontinue the study early, should return for observational follow-up visits four, eight and fourteen weeks after the last dose of IP.

Intervention

- Placebo-controlled Treatment Phase - Weeks 0 to16:
Subjects will be randomly assigned in a 2:1 ratio to weight-based apremilast or placebo. Subjects 20 kg to < 50 kg will receive apremilast 20 mg BID or placebo BID and subjects >= 50 kg will receive apremilast 30 mg BID or placebo BID.

- Apremilast Extension Phase - Weeks 16 to 52
Placebo subjects will be switched at Week 16 to receive apremilast 20 mg BID or 30 mg BID, according to baseline weight. All other subjects will continue to receive either apremilast 20 mg BID or apremilast 30 mg BID based on their original dosing assignment.

- Observational Follow-up Phase - 14 weeks

Study burden and risks

Apremilast is an investigational drug and some side effects may still be unknown. There is always a risk when the patient takes any treatment, including the possibility of death. Patients will be carefully watched during the study for any side effects or problems. Some side effects go away soon after the patient stops the study treatment. In some cases, side effects can last a long time. Sometimes they may not go away. Patients/parents of patients should tell the study doctor/staff about anything that is bothering them or any side effects that they may have, even if they do not think they are related to the study medicine.

Apremilast may cause all, some or none of the side effects listed below. These side effects can be mild but could also be serious, life-threatening or even result in death. Patients may also experience an allergic reaction that has not been seen before.

The following list of side effects includes ones that may be associated with the use of apremilast:
• Very Common (which may affect more than 1 person in 10): diarrhea, nausea (stomach upset) and headache, upper respiratory tract infection (infections of the nose, throat and airways).
If you become dehydrated or experience low blood pressure, you may be at a higher risk of complications. If you experience severe diarrhea, nausea, or vomiting please notify your study doctor immediately.
• Common (which may affect between 1 and 10 people in every 100): upper abdominal (stomach) pain, indigestion, frequent bowel movement, heartburn,

vomiting, fatigue, bronchitis (infection of the tubes to the lungs), Nasopharyngitis (common cold), decreased appetite, back pain, tension, headache (and migraine), difficulty sleeping, depression, cough.
If you have a history of depression and/or suicidal thoughts or behavior, please tell your study doctor. If you have any symptoms of depression or if your depression becomes worse, or if you have suicidal thoughts or other mood changes, contact your study doctor immediately.
• Uncommon (which may affect between 1 and 10 people in every 1000): allergic reaction, rash, weight loss.

Risks from the Study Procedures:
Patients/parents of patients should let the study doctor know if they have any allergies, including allergies to latex or adhesives, as they may become exposed to these (in treatment gloves or bandages) while having study procedures.
• Blood Tests: Possible side effects of having blood drawn are tenderness, pain, bruising, bleeding, and/or infection where the needle goes into the skin and blood vein. Having blood drawn may also cause patients to feel nauseated and/or lightheaded.
In total, we will take about 100 ml of blood from you (5-7 ml of blood each time). This amount does not cause any problems in children. To compare: a blood donation involves 500 ml of blood being taken each time.
• Blood Pressure: Although it is very rare, patients might bruise from having their blood pressure taken. Also, the blood pressure cuff will be very tight and might pinch a little for a short time.

Risks from using apremilast in combination with other drugs:
Patients/parents of patients should the study doctor or the study staff about any drugs they are taking, have recently taken, or are planning to take, including herbal remedies, supplements, and drugs you take without a prescription. The side effects of using apremilast in combination with other drugs are unknown at this time.

As of 20 March 2020, approximately 8300 patients have received apremilast in research studies. Since it was first approved for sale in March 2014, approximately 485.000 people have been prescribed apremilast for the treatment of psoriasis, psoriatic arthritis and Behcet*s disease.

Reports of various types of cancers, cardiac disorders (heart problems), stroke and serious infections have been observed in apremilast studies. However, these events occurred at a similar rate between patients taking apremilast and those taking placebo (sugar pill).
In clinical studies, weight loss has been observed. If you experience unintentional or unexplained weight loss (for example, if you have weight loss without actively trying to lose weight), please notify your study doctor immediately.
Inflammation of the vessels was seen when apremilast was given to mice and

rarely reported in humans. If you notice swelling, pain, or tenderness, please tell your study doctor.

It is possible that the condition for which patients are being treated may get worse during the study. Patients will be monitored closely. If their condition gets worse, the investigator will stop their participating in this study. The doctor will treat the patients as he / she thinks is best.

Contacts

Public
Amgen

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Scientific
Amgen

One Amgen Center Drive
Thousand Oaks, CA 91320
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Males or female subjects 6 to 17 years of age, inclusive, at the time the informed consent form is signed by the legal guardian

2. Subjects must have a weight of >= 20 kg
3. Subject must have age and sex-specific BMI value no lower in range than the 5th percentile on the Centers for Disease Control (CDC) growth chart for children and adolescents.
7. Diagnosis of chronic plaque psoriasis for at least 6 months prior to Screening.
8. Has moderate to severe plaque psoriasis at Screening and Baseline as defined by:
• PASI score >= 12; and
• Body surface area (BSA) >= 10%; and
• sPGA >= 3 (moderate to severe)
9. Disease inadequately controlled by or inappropriate for topical therapy for psoriasis
10. Candidate for systemic therapy or phototherapy
11. At Screening, laboratory values must be within the following ranges:
White blood cell (WBC) count: (Age 6-18 years; Males/Females 3.5 - 13.5 x 10E3 /µL)
Platelet count (Age 6-18 years; Males/Females 125 - 500 x 10E3 /µL)
Serum creatinine <= 1.2 x upper-limit of normal (ULN) for age and gender.
AST and ALT <= 1.5 x ULN for age and gender. If initial test of ALT or AST is > 1.5 x ULN, one repeat test is allowed during Screening.
Total bilirubin <= 2 mg/dL (<= 34 µmol/L). If initial test result is > 2 mg/dL, one repeat test is allowed during the Screening period
Hemoglobin (Hb) Age (years) - Males (g/dL) - Females (g/dL)
6-11: 10.0-15.0 - 10.0-15.0
12-18: 11.0-16.5 - 10.5-15.5
12. All females of childbearing potential must either practice abstinence from heterosexual contact or use one of the approved contraceptive options as described in the protocol while on apremilast and during any dose interruption, and for at least 28 days after administration of the last dose of apremilast.
For the purpose of this study, a female subject is considered of childbearing potential if she is >= 12 years old or has reached menarche, whichever occurred first.
Females of childbearing potential must have a negative pregnancy test at Screening and Baseline.

Exclusion criteria

1. Other than psoriasis, history of any clinically significant (as determined by the Investigator) cardiac, endocrinologic, pulmonary, neurologic, psychiatric, hepatic, renal, hematologic, immunologic disease, or other major uncontrolled disease.
2. Any condition, including the presence of laboratory abnormalities, or psychiatric illness, that would place the subject at unacceptable risk if he/she were to participate in the study

3. Any condition that confounds the ability to interpret data from the study.
4. Evidence of skin conditions, other than psoriasis, that would interfere with clinical assessments
6. Guttate, erythrodermic, or pustular psoriasis at Screening and Baseline
7. Psoriasis flare or rebound within 4 weeks prior to Screening
8. Positive Hepatitis B surface antigen, or anti-hepatitis C antibody, at Screening
9. History of positive human immunodeficiency virus infection (HIV), congenital and acquired immunodeficiencies (eg, common variable immunodeficiency, immunoglobulin A deficiency)
10. Active tuberculosis (TB) or a history of incompletely treated TB
11. History of recurrent significant infections
12. Active infection or infection treated with antibiotic treatment within 2 weeks of first dose
13. Any history of or active malignancy
14. History of allergy/intolerance to any component of the investigational product, ie, apremilast, lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate,
hypromellose 15cP, titanium dioxide, polydextrose food chemical color, talc, maltodextrine, medium chain triglycerides, iron oxide red, iron oxide yellow, and iron oxide black.
15. Deficiencies in lactose metabolism, ie, galactose-1-phosphate uridylyltransferase, UDP-galactose 4-epimerase, galactokinase or Fanconi Bickel syndrome, including congenital lactase deficiencies, and glucose-galactose malabsorption.
16. Prior history of suicide attempt at any time in the subject's lifetime prior to Screening or randomization in the study, or major psychiatric illness requiring hospitalization within 3 years prior to signing the assent and informed consent
17. Answer Yes to any question on the Columbia-Suicide Severity Rating Scale during Screening or at Baseline
18. Current or planned concurrent use of the following therapies that may have a possible effect on psoriasis
a. Topical therapy within 2 weeks prior to randomization (including but not limited to topical corticosteroids, topical retinoid or vitamin D analog preparations, tacrolimus, pimecrolimus, or anthralin/dithranol)
Exceptions*
i. Low potency or weak corticosteroids (please refer to the Investigators' Manual) will be allowed as background therapy for treatment of the face, axillae and groin in accordance with manufacturer's suggested usage
ii. Unmedicated skin moisturizer (eg, Eucerin®) will also be permitted for body lesions
*Subjects should not use these topical treatments within 24 hours prior to the clinic visit.
b. Conventional systemic therapy for psoriasis within 4 weeks prior to randomization (including but not limited to cyclosporine, corticosteroids, methotrexate, oral retinoids, mycophenolate, thioguanine, hydroxyurea,

sirolimus, sulfasalazine, azathioprine, and fumaric acid esters)
c. Phototherapy treatment (ie, ultraviolet B [UVB], PUVA) within 4 weeks prior to randomization
d. Biologic therapy:
i. Etanercept (or biosimilar) treatment four weeks prior to randomization
ii. Adalimumab (or biosimilar) treatment ten weeks prior to randomization
iii. Other TNF or IL-17 blockers (such as infliximab, certolizumab pegol, secukinumab, ixekizumab, brodalumab, or their biosimilars) within 12 weeks prior to randomization
iv. Anti-IL-12 or anti-IL-23 treatment (such as ustekinumab, guselkumab, or tildrakizumab) within 24 weeks prior to randomization
e. Use of any investigational drug within 4 weeks prior to randomization, or 5 pharmacokinetic/pharmacodynamic half-lives, if known (whichever is longer)
19. Prolonged sun exposure or use of tanning booths or other ultraviolet (UV) light sources
20. Children in Care: a child who has been placed under the control or protection of an agency, organization, institution or entity by the courts, the government or a government body, acting in accordance with powers conferred on them by law or regulation
21. Prior treatment with apremilast

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	26-02-2020
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Otezla
Generic name:	apremilast
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-01-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-07-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-01-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-01-2020
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-02-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-07-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-12-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-04-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-05-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-06-2021
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-09-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2018-002918-12-NL
ClinicalTrials.gov	NCT03701763,U1111-1219-3112
CCMO	NL67710.091.18

Study results

Date completed:	24-11-2021
Results posted:	22-12-2023

First publication
18-09-2023