A phase 4, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of apremilast (CC-10004) in subjects with early, oligoarticular psoriatic arthritis despite initial stable treatment with either non-steroidal anti-inflammatory drugs (NSAIDs) and/or <=1 conventional synthetic disease-modifying antirheumatic drugs (DMARD).

Published: 20-11-2018
Last updated: 10-01-2025

Primary Objective• To evaluate the efficacy of apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo * NSAIDs and/or csDMARDs in subjects with early oligoarticular PsA, assessed by modified MDA (MDA-Joints).Secondary Objectives · To evaluate the...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON48290

Source
ToetsingOnline

Brief title
Celgene CC-10004-PSA-013

Condition

- Autoimmune disorders

Synonym
oligoarticular psoriatic arthritis; Joint inflammation affecting individuals with the skin disorder

Research involving
Human

Sponsors and support

Primary sponsor: Celgene Corporation
Source(s) of monetary or material Support: Celgene Corporation

Intervention

Keyword: Apremilast, CC-10004, disease-modifying antirheumatic drugs (DMARD), oligoarticular psoriatic arthritis

Outcome measures

Primary outcome

Modified Minimal Disease Activity (MDA-Joints): Based on achieving < 1 swollen joint count (SJC) and < 1 tender joint count (TJC; 66/68 SJ/TJ counts), plus 3 out of 5 of the following cut-off values: Body Surface Area (BSA) < 3%, Patient pain assessment, (Visual analog scale [VAS] < 15, Patient global assessment of disease activity (VAS) < 20, HAQ < 0.5, Tender entheseal points < 1 (Based on the Leeds Enthesitis Index - LEI).

Secondary outcome

- cDAPSA remission or low disease activity: Proportion of subjects who achieve remission (defined by clinical disease activity in psoriatic arthritis [DAPSA] <= 4 score) or low disease activity (defined by cDAPSA > 4 but <= 13 score).

- Swollen Joint Count (SJC)<= 1: Proportion of subjects with SJC <= 1.

- Tender Joint Count (TJC))<= 1: Proportion of subjects with TJC <= 1

- Patient's assessment of pain: Proportion of subjects whose assessment of pain

improves to <=15 in VAS.

- PsAID-12: Change from Baseline in the Psoriatic Arthritis Impact of Disease

12-item for clinical trials (PsAID-12) questionnaire.

- PASDAS good and moderate response: Proportion of patients achieving a good or

moderate response in PASDAS score.

Study description

Background summary

Psoriatic arthritis (PsA) is a heterogeneous inflammatory rheumatologic disorder characterized by inflammatory arthritis affecting 6% to 39% of patients suffering from psoriasis. PsA is classified as a seronegative spondyloarthropathy (SpA) because it shares certain features with other conditions included in that group. Indeed, spinal involvement has been reported in up to 50% of patients with PsA. In addition, PsA is associated with enthesitis and dactylitis, which are common to SpA. Finally, the majority of patients with PsA are negative for rheumatoid factor (RF).

Apremilast (CC-10004) is an oral phosphodiesterase enzyme (PDE) inhibitor. It is highly selective for PDE4, which is the dominant PDE in inflammatory cells. Through inhibiting PDE4, apremilast elevates intracellular cyclic adenosine monophosphate (cAMP) levels, leading to a partial inhibition of the production of many pro-inflammatory mediators, as well as an increase in some anti-inflammatory mediators.

Apremilast has been shown to be safe and efficacious in reducing signs and symptoms of PsA, as well as improving physical function. Like most agents, the clinical development program of apremilast was restricted to subjects with >= 3 swollen and >= 3 tender joints at baseline. This allowed for a limited proportion of subjects with asymmetric oligoarthritis at study entry. Consequently, the safety and efficacy of apremilast in patients with oligoarthritis remains to be further investigated.
The current study is designed to evaluate the benefit:risk profile of apremilast in subjects with an early diagnosis of PsA (* 24 months), presenting with oligoarthritis, despite initial stable treatments with either NSAIDs

and/or * 1 csDMARD (methotrexate [MTX] or sulfasalazine [SSZ].

Study objective

Primary Objective
• To evaluate the efficacy of apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo * NSAIDs and/or csDMARDs in subjects with early oligoarticular PsA, assessed by modified MDA (MDA-Joints).
Secondary Objectives
· To evaluate the impact of treatment with apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo *NSAIDs and/or csDMARDs on disease activity in subjects with early oligoarticular PsA,
· To evaluate the impact of apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo * NSAIDs and/or csDMARDs on patient reported outcomes (PROs) in subjects with early oligoarticular PsA,
· To evaluate the safety and tolerability of apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo * NSAIDs and/or csDMARDs in subjects with early oligoarticular PsA.
Exploratory Objectives
· To evaluate the impact of treatment with apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo *NSAIDs and/or csDMARDs on clinical efficacy outcomes related to psoriatic arthritis disease in subjects with early oligoarticular PsA.
· To evaluate the impact of apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo * NSAIDs and/or csDMARDs on health-related quality of life (HRQoL) outcome measures in subjects with early oligoarticular PsA,
· To evaluate the impact of treatment with apremilast 30 mg BID * NSAIDs and/or csDMARDs vs. Placebo *NSAIDs and/or csDMARDs on Body Mass Index (BMI), waist circumference and glycated hemoglobin (HbA1c) in subjects with early oligoarticular PsA.

Study design

This is a Phase 4, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety and tolerability of apremilast (CC-10004) in subjects with early (>= 3 months 24 months since diagnosis) oligoarticular PsA, despite treatment with either NSAIDs and/or 1 csDMARD. Approximately 330 subjects will be randomized (2:1) to apremilast 30 mg BID or placebo

Intervention

Eligible subjects will enter the Placebo-controlled Phase at the Baseline Visit. Subjects will be assigned randomly to apremilast 30 mg twice daily (BID) or placebo BID. Subjects are to take investigational product (IP), as designated in the treatment card, twice daily (morning and evening,

approximately 12 hours apart, with or without food).
With the aim to mitigate potential dose-related side effects associated with apremilast, such as headache and gastrointestinal (GI) disturbances, apremilast-treated subjects will be dose-titrated from 10 mg BID to 20 mg BID to 30 mg BID over the first 5 days of treatment. Subjects assigned to placebo will receive 10-, 20-, and 30-mg placebo tablets in blister cards (treatment cards) which are identical in appearance to the corresponding strength apremilast tablets. Apremilast will be provided in blister cards as either 10 mg, 20 mg or 30 mg tablets. The 5-day titration period will also be initiated for the placebo arm after the following visits: Baseline, Week 16 (early escape) and Week 24. The original treatment assignments (apremilast 30 mg BID or placebo) will remain blinded throughout the study.
At the Week 16 Visit, subjects with no improvement in SJC (sentinel joints) at Week 16 are eligible for early escape, at the discretion of the Investigator and will receive early escape treatment with apremilast 30 mg BID. The joints monitored for early escape must correspond to those affected at the Baseline Visit (sentinel joints).

Study burden and risks

This is a Phase 4, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety and tolerability of apremilast (CC-10004) in subjects with early (>= 3 months 24 months since diagnosis) oligoarticular PsA, despite treatment with either NSAIDs and/or 1 csDMARD. Approximately 330 subjects will be randomized (2:1) to apremilast 30 mg BID or placebo. Patients are asked to undergo procedures described on pages 54-57 of the study protocol. These procedures include physical examination, joint examination, nail examination, vital signs, height measurement, weight measurement, diarrhea assessment, blood and urine sampling, completion of questionnaires, answer questions of investigators and study team and study drug intake as directed. Additionally, fertile subjects are asked to use contraceptives, and female subjects of childbearing potential will have pregnancy tests.
Apremilast has been shown to be safe and efficacious in reducing signs and symptoms of PsA, as well as improving physical function. Like most agents, the clinical development program of apremilast was restricted to subjects with >= 3 swollen and >= 3 tender joints at baseline. This allowed for a limited proportion of subjects with asymmetric oligoarthritis at study entry. Consequently, the safety and efficacy of apremilast in patients with oligoarthritis remains to be further investigated.
The current study is designed to evaluate the benefit:risk profile of apremilast in subjects with an early diagnosis of PsA (< 24 months), presenting with oligoarthritis, despite initial stable treatments with either NSAIDs and/or < 1 csDMARD (methotrexate [MTX] or sulfasalazine [SSZ].

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

1. 1. Subject is a male or female, >= 18 years at time of consent.
2. Subjects must understand and voluntarily sign an informed consent document prior to any study related assessments/procedures being conducted.
3. Subject is willing and able to adhere to the study visit schedule and other protocol requirements.
4. Subject must have a documented diagnosis of PsA (by any criteria) of >= 3 months but <= 24 months duration at the time of the Screening Visit.
5. Subject meets the CASPAR (Appendix B) criteria for PsA at the Screening Visit.
6. Subject must have a total number of swollen joints greater than 1 and equal or less than 4 (> 1 but < 4 swollen joints) at the Screening Visit and confirmed prior to randomization at the Baseline Visit.

7. Subject must have a total number of tender joints greater than 1 and equal or less than 4 (> 1 but < 4 tender joints) at Screening and confirmed prior to randomization at the Baseline Visit.
8. Subjects taking oral glucocorticosteroids must be on a stable dose of prednisone <= 10 mg/day or equivalent for at least 4 weeks prior to the Baseline Visit (Section 8.1).
9. For all regions, the local Regulatory Label for treatment with apremilast must be followed. For example, subjects in the EU must have had inadequate response or intolerance to a prior csDMARD.
10. Subjects taking 1 protocol-allowed csDMARD (methotrexate [MTX] or sulfasalazine [SSZ]) may enter the study provided that the duration of treatment is <=6 months prior to the Baseline Visit and treatment is taken at a stable dose for at least 3 months prior to the Baseline Visit. See Permitted Medications (Section 8.1) for details describing dose criteria.
11. Subjects exposed to MTX or SSZ and stopped treatment due to intolerance or due to safety reasons may enter the study provided that treatment was stopped within at least 4 days of the Baseline Visit.
12. Subjects taking NSAIDs may enter the study provided that the dose is stable for at least 2 weeks prior to the Baseline Visit. Subjects may discontinue NSAIDs at any time up to and including the Baseline Visit, prior to study randomization.
13. Females of childbearing potential (FCBP*) must have a negative pregnancy test at Screening and the Baseline Visit. While on investigational product and for at least 28 days after taking the last dose of investigational product, FCBP who engage in activity in which conception is possible must use one of the approved contraceptive** options described below:
Option 1: Any one of the following highly effective methods: hormonal contraception (oral, injection, implant, transdermal patch, vaginal ring); intrauterine device (IUD); tubal ligation; or partner*s vasectomy;
OR
Option 2: Male or female condom (latex condom or non-latex condom NOT made out of natural [animal] membrane [for example, polyurethane]); PLUS one additional barrier method: (a) diaphragm with spermicide; (b) cervical cap with spermicide; or (c) contraceptive sponge with spermicide.
NOTE: Option 2 may not be acceptable as a highly effective contraception option in all countries per local guidelines/regulations.
*A female of childbearing potential is defined as a sexually mature female who: 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or 2) has not been postmenopausal for at least 24 consecutive months (that is, has had menses at any time during the preceding 24 consecutive months).
**The female subject*s chosen form of contraception must be effective by the time the female subject is screened into the study (for example, hormonal contraception should be initiated at least 28 days before screening).
14. Must be in general good health (except for psoriatic arthritis) as judged by the Investigator, based on medical history, physical examination, and clinical laboratories. (Note: The definition of good health means a subject

does not have uncontrolled significant comorbid conditions).

Exclusion criteria

1.1. Prior use of >1 cs DMARD.
2. Prior exposure to a JAK-inhibitor, including tyk2 inhibitors and/or a biologic DMARD.
3. Use of intra-articular (IA) or intra muscular (IM) glucocorticoid injection within 8 weeks before the Baseline Visit.
4. Use of leflunomide within 12 weeks of randomization. Subjects who stopped leflunomide and completed 11 days of treatment with cholestyramine (8 g, 3 x daily) prior to the Baseline Visit may enter the study.
5. Prior use of cyclosporine.
6. Prior treatment with apremilast, or participation in a clinical study, involving apremilast.
7. Use of any investigational drug within 4 weeks of the Baseline Visit, or 5 pharmacokinetic/pharmacodynamic half-lives, if known (whichever is longer).
8. History of clinically significant or uncontrolled disease (as determined by the Investigator), which places the subject at unacceptable risk if he/she were to participate in the study.
9. Any condition, including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study. Subjects with a creatinine clearance level less than 30 mL/min (estimated by the Cockcroft-Gault equation) will be considered to have severe renal impairment and will be excluded from the study.
10. Prior history of suicide attempt at any time in the subject's lifetime prior to signing the informed consent, or major psychiatric illness requiring hospitalization within the last 3 years prior to signing the informed consent.
11. Pregnant or breast feeding.
12. Active substance abuse or a history of substance abuse within 6 months prior to Screening.
13. History of allergy or hypersensitivity to any component of the investigational product.
14. History of positive human immunodeficiency virus (HIV), or congenital or acquired immunodeficiency (eg, Common Variable Immunodeficiency Disease).
15. Active tuberculosis or a history of incompletely treated tuberculosis.
16. Bacterial infections requiring treatment with oral or injectable antibiotics, or significant viral or fungal infections, within 4 weeks of Screening. Any treatment for such infections must have been completed and the infection cured, at least 4 weeks prior to Screening and no new or recurrent infections prior to the Baseline Visit.
17. Malignancy or history of malignancy or myeloproliferative or lymphoproliferative disease within the past 3 years, except for treated (ie, cured) basal cell or squamous cell in situ skin carcinomas.
18. Major surgery (including joint surgery) within 8 weeks prior to the

Screening Visit or planned major surgery within 6 months following the Baseline Visit.
19. Rheumatic autoimmune disease other than PsA, including, but not limited to: systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), scleroderma, polymyositis, or fibromyalgia.
20. Prior history of or current inflammatory joint disease other than PsA (eg, gout, reactive arthritis, rheumatoid arthritis [RA], ankylosing spondylitis, Lyme disease), which confounds the ability to interpret data from the study.
21. Erythrodermic, guttate, or generalized pustular psoriasis at randomization.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	20-11-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-06-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-07-2020
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	EUCTR2018-002735-26-NL
ClinicalTrials.gov	NCT03747939
CCMO	NL67713.078.18

Study results

Results posted: 20-03-2024

Summary results
Trial never started

First publication
18-09-2023