Phase 3, Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel Group Study to Evaluate the Efficacy, Safety and Pharmacokinetics of Apremilast in Children From 5 to Less Than 18 Years of Age With Active Juvenile Psoriatic Arthritis (PEAPOD)

Published: 18-02-2021
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This study has been transitioned to CTIS with ID 2023-503435-17-00 check the CTIS register for the current data. Estimate the efficacy of apremilast compared with placebo in the treatment of Juvenile Psoriatic Arthritis (JPsA) in pediatric subjects...

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

Summary

ID

NL-OMON51888

Source
ToetsingOnline

Brief title
20190529 PEAPOD

Condition

- Autoimmune disorders
- Joint disorders
- Epidermal and dermal conditions

Synonym
Inflammation of skin and joints, Psoriatic Arthritis in children

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Apremilast, Inflammation of skin and joints, Juvenile Psoriatic Arthritis, pediatric study

Outcome measures

Primary outcome

The primary outcome of the study is to assess the number of patients achieving

ACR Pedi 30 response at week 16

Secondary outcome

- Change in subject's assessment of pain (visual analog scale [VAS]) from

baseline (week 0) to week 16;

- Number of participants achieving ACR Pedi 20/50/70/90 from baseline (week 0)

to week 16;

- Change in Childhood Heath Assessment Questionnaire (CHAQ) from baseline (week

0) to week 16;

- Change in Juvenile Arthritis Disease Activity Score (JADAS) from baseline

(week 0) to week 16;

- Number of participants who experience PsA flares from baseline (week 0) to

week 16;

- Psoriasis Area Severity Index (PASI)-75 response at week 16 for subjects with

a baseline psoriasis body surface area (BSA) equal or more than 3%;

- Number of participants who experience treatment-emergent adverse events (type, frequency, severity and relationship to apremilast) from baseline (week 0) to week 56;

- Number of participants who experience clinically significant laboratory tests, vital sign or physical examination measurements from baseline (week 0) to week 56;

- Occurrence, severity, and frequency of suicide/suicide-related ideations and behaviors as assessed by the Columbia-Suicide Severity Rating Scale (C-SSRS) Questionnaire from baseline(week 0) to week 56;

- Body weight, height and body mass index (BMI) from baseline (week 0) to week 56;

- Tanner Staging Assessment of sexual maturity at baseline (week 0) and week 52 (or Early Termination visit);

- Plasma concentrations of apremilast from week 2 to week 52 (or Early Termination visit);

- Taste and acceptability at baseline (week 0) and week 2.

Study description

Background summary

Juvenile PsA is highly heterogeneous, characterized by arthritis and rash, nail changes (including pitting, onycholysis, and oil-drop sign), and uveitis.
Juvenile PsA resembles adult PsA. However, unlike adult PsA, inflammatory arthritis precedes skin psoriasis in about half of children with JPsA.
The Investigational study drug, Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate

(cAMP). PDE4 inhibition results in increased intracellular cAMP levels, which in turn modulates a network of pro- and anti inflammatory mediators. Through targeted PDE4 inhibition, apremilast reduces the inflammatory response implicated in inflammatory and autoimmune disorders. Apremilast, is marketed worldwide under trade name Otezla® (30mg BID). It is approved for both psoriatic arthritis and psoriasis in 54 countries including the United States (US) and member states of the European Union (EU).
Refer to section 2.1 and 2.2 of the protocol for more information.

Study objective

This study has been transitioned to CTIS with ID 2023-503435-17-00 check the CTIS register for the current data.

Estimate the efficacy of apremilast compared with placebo in the treatment of Juvenile Psoriatic Arthritis (JPsA) in pediatric subjects 5 to less than 18 years of age.
Refer to section 3 of the protocol for more information.

Study design

This is a phase 3, multicenter, randomized, parallel group study with a double-blind, placebo-controlled phase followed by an active treatment phase to assess the efficacy, safety, tolerability, and pharmacokinetics of apremilast in subjects aged 5 to < 18 years with active Juvenile Psoriatic Arthritis (JPsA). The total study duration for an individual subject is 62 weeks, comprising up to a 6 week screening phase, a 52 week treatment phase (16 week double-blind, placebo-controlled treatment phase and 36 week apremilast active treatment phase), and a 30 day posttreatment safety follow-up phase for subjects who are not continuing to receive apremilast through the Post-Trial Access Program.

The double-blind, placebo-controlled treatment phase will be 16 weeks in duration (week 0 to week 16). At least 60 evaluable subjects will be randomized in a 2:1 ratio on day 1 to oral apremilast (tablet or liquid suspension) or placebo (tablet or liquid suspension). The randomization will be stratified by formulation (tablet or liquid formulation) with approximately 30 subjects stratified to each formulation. Subjects will be dose titrated during the first week to mitigate gastrointestinal adverse events. Subjects >= 15 kg to < 20 kg and subjects who have a known or documented inability to swallow a tablet will be randomized to the apremilast or placebo liquid suspension formulation.

The apremilast active treatment phase will be 36 weeks in duration (week 16 to week 52). To maintain the blinded condition of the treatments, all subjects will be dose titrated when they enter the active treatment phase. Subjects assigned to apremilast treatment during the double-blind, placebo-controlled

treatment phase will continue to receive the same apremilast formulation and original assigned dose following the dose titration. Subjects who were assigned to placebo treatment during the double-blind, placebo-controlled treatment phase will be switched at week 16 to receive apremilast tablet or liquid solution with corresponding dose regimen according to baseline weight following the dose titration.

To increase retention rates in subjects who experience limited benefit after 8 weeks of receiving investigational product (IP), considering that many or most of these pediatric patients will wash out their prior medications at least 2 weeks before Day 1 of the study, an early escape option will be implemented. Starting at week 8, at the discretion of the investigator, subjects demonstrating no improvement from baseline in at least 3 of the 6 ACR Pedi core criteria and no more than 1 of the 6 ACR Pedi core criteria with >= 30% improvement will be eligible for early escape. Placebo-treated subjects who early escape will be transitioned to apremilast based on their body weight (at baseline), while apremilast-treated subjects will remain on their original treatment assignment. All subjects participating in early escape will be assigned as non-responders at week 16.

Upon completion of investigational product administration subjects will be followed for safety.
The 30 (+ 3) day posttreatment follow-up phase is considered sufficient to assess rebound effects and to evaluate safety given the half-life of apremilast (6 to 9 hours).

Intervention

Week 0 to week 16 - double-blind, placebo-controlled treatment phase:
- one group will receive apremilast depending on weight (10 mg BID for >= 15 kg to < 20 kg, 20 mg BID for >= 20 kg to < 50 kg and 30 mg BID for >= 50 kg)
- other group will receive placebo

Week 16 to week 52 - active treatment phase:
- all patients will receive apremilast depending on weight (10 mg BID for >= 15 kg to < 20 kg, 20 mg BID for >= 20 kg to < 50 kg and 30 mg BID for >= 50 kg)

Study burden and risks

Refer to section E9 en E9a.

Contacts

Public

Amgen

Minervum 7061
Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or Female subjects 5 to < 18 years of age at the time of randomization.
• Subject must have a confirmed diagnosis of JPsA according to the International League of Associations for Rheumatology (ILAR) Edmonton Revision (Petty, 2001) classification criteria of at least 6 months duration:
o Arthritis and psoriasis, OR
o Arthritis with at least 2 of the following:
* Dactylitis
* Nail pitting or onycholysis
* Psoriasis in a first-degree relative
• Active disease: at least 3 active joints (including distal interphalangeal joints).
• Inadequate response (at least 2 months) or intolerance to >= 1 DMARD, (which may include MTX or biologic agents).
Inclusion criteria are described in more detail in section 5.1 of the protocol.

Exclusion criteria

• Exclusions per ILAR Edmonton Revision (Edmonton, 2001) criteria for JPsA include:
o Arthritis in an HLA-B27-positive male with arthritis onset after 6 years of age
o Ankylosing spondylitis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, acute anterior uveitis, or a history of one of these disorders in a first-degree relative
o History of IgM rheumatoid factor on at least 2 occasions at least 3 months apart
o Presence of systemic JIA.
• Rheumatic autoimmune disease other than PsA, including, but not limited to: systemic lupus erythematosus, mixed connective tissue disease, scleroderma, polymyositis, or fibromyalgia.
• Prior history of or current inflammatory joint disease other than PsA (eg, gout, reactive arthritis, rheumatoid arthritis, ankylosing spondylitis, Lyme disease).
Exclusion criteria are described in more detail in section 5.2 of the protocol.

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:	Pending
Start date (anticipated):	01-04-2023
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Generic name:	Press-In Bottle Adapter (PIBA)
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Otezla
Generic name:	Apremilast
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-02-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	23-09-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	05-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-09-2023
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
EU-CTR	CTIS2023-503435-17-00
EudraCT	EUCTR2019-002788-88-NL
ClinicalTrials.gov	NCT04804553
CCMO	NL75123.041.21