A Phase 3, Multicenter, Randomized, Placebo- and Active Comparator-Controlled Study Evaluating the Efficacy, Safety, and Pharmacokinetics (PK) of Subcutaneously Administered Guselkumab for the Treatment of Chronic Plaque Psoriasis in Pediatric Subjects (>=6 To <18 Years of Age)

Published: 06-06-2018
Last updated: 12-04-2024

Primary ObjectivesThe primary objective of this study is to evaluate the efficacy and safety of guselkumab in pediatric participants aged >=6 through =6 through =6 through

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

Summary

ID

NL-OMON52759

Source
ToetsingOnline

Brief title
PROTOSTAR

Condition

- Autoimmune disorders
- Epidermal and dermal conditions

Synonym
skin disease

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: door de verrichter

Intervention

Keyword: guselkumab, paediatrics, plaque psoriasis

Outcome measures

Primary outcome

Efficacy evaluations include:

• Investigator*s Global Assessment (IGA)

• Psoriasis Area and Severity Index (PASI)

• Body Surface Area (BSA)

• Children*s Dermatology Life Quality Index (CDLQI)

• Family Dermatology Life Quality Index (FDLQI)

Secondary outcome

The co-primary and major secondary endpoints for Part 1, with the primary

comparisons between the guselkumab and placebo groups, include:

Co-primary Endpoints

• The proportion of participants achieving an IGA score of cleared (0) or

minimal (1) at Week 16.

• The proportion of participants with a PASI 75 response at Week 16.

Major Secondary Endpoints

• The proportion of participants achieving a PASI 90 response at Week 16.

• The proportion of participants achieving an IGA score of cleared (0) at Week 16.

• The proportion of participants achieving a PASI 100 response at Week 16.

• The change from baseline in CDLQI at Week 16.

Other Secondary Endpoints

Secondary endpoints for Part 1 of the study include:

• The proportion of retreated participants that achieve a PASI 90 response over time after retreatment.

• The proportion of retreated participants that achieve PASI responses (PASI 50, 75, 90, and 100) or IGA responses (IGA of cleared [0], minimal [1], or mild [2], IGA of cleared [0] or minimal [1], and IGA of cleared [0]) over time after retreatment.

• The time to loss of 50% of the Week 16 PASI improvement (ie, time to retreatment) after withdrawal.

• The time to loss of PASI 90 response after withdrawal.

• The proportion of participants achieving a PASI 50 response at Week 16.

• The proportion of participants who achieve an IGA score of mild or better (<=2) at Week 16.

• The percent improvement from baseline in PASI over time through Week 16.

• The proportion of PASI responses (PASI 50, 75, 90, and 100) over time through Week 16.

• The proportion of IGA responses (IGA of cleared [0], minimal [1], or mild [2], IGA of cleared [0] or minimal [1], and IGA of cleared [0]) over time through Week 16.

• The proportion of participants with CDLQI=0 or 1 at Week 16 among randomized participants with a baseline CDLQI>1

• Body surface area involved (BSA) and change from baseline in BSA at Week 16 will be compared between the guselkumab group and the placebo group.

• BSA and change from baseline in BSA will be summarized over time through Week 16.

• The proportion of participants with FDLQI=0 or 1 at Week 16 among randomized participants with a baseline FDLQI>1.

• The change from baseline in FDLQI at Week 16.

For Part 2 of the main study, PASI responses, IGA responses, PASI percent improvement, change from baseline in CDLQI and FDLQI, the proportion of participants achieving a CDLQI of 0 or 1, and the proportion of participants achieving a FDLQI of 0 or 1 will be summarized over time through Week 52.

Study description

Background summary

Plaque psoriasis is a chronic, immunologically-mediated, inflammatory skin disease of unknown etiology affecting 2% to 4% of the general population. The pathogenesis of plaque psoriasis involves environmental factors and immune dysregulation in genetically-predisposed individuals. Substantial evidence indicates that IL-23 plays an important role in innate and adaptive immune responses, and may play a pivotal role in the pathogenesis of psoriasis vulgaris.
Adult and pediatric plaque psoriasis share similar clinical manifestations,

histological features, genetic factors, and treatment options.6 Taken together, the data demonstrate that a complex network of immune mediators (cells and cytokines) drive the inflammatory skin processes of plaque psoriasis in adults and children.
Plaque psoriasis is characterized by symmetrically distributed, well-defined, sharply demarcated, indurated, erythematous plaques that are covered by friable, dry, white-silvery scale and is reported to account for up to 84% of psoriasis in pediatric patients. Areas of the body that are frequently involved include the scalp, elbows, knees, buttocks, and genitalia. Definitions of plaque psoriasis severity differ depending on the source, but are generally related to the extent of the body surface involved, although the extent of exposed skin involved is also often considered.
Studies addressing the age of onset of psoriasis have suggested that 2 subgroups exist: early onset disease (before 30 years of age, including pediatric onset) and late onset disease (after age 30). Generally, the clinical manifestations of plaque psoriasis in patients with pediatric onset and those with adult or late onset disease are similar, and not clinically distinguishable. Therefore, the consensus of the literature is essentially that plaque psoriasis is a life-long chronic disease with a variable age of onset, and that pediatric plaque psoriasis is probably most accurately characterized as early onset disease rather than as an entity distinct from adult plaque psoriasis.
The traditional paradigm for the treatment of plaque psoriasis follows a stepwise approach to treatment starting with topical agents, followed by phototherapy, and then systemic agents. Recently, several biologic psoriasis treatments have been approved for use in patients with pediatric plaque psoriasis. Currently, etanercept (ENBREL®), adalimumab (HUMIRA®) and ustekinumab (STELARA®) are approved for various pediatric age groups in some jurisdictions. Among these biologics, etanercept is currently approved in a broad pediatric age range and the largest number of geographic regions.
Although stepwise therapy is mentioned frequently in the literature, the optimal treatment approach for pediatric patients with chronic plaque psoriasis is far less clear than for adults due to the practical scheduling issues of phototherapy in school aged children, the known, often cumulative, toxicities of traditional systemic therapies and the paucity of rigorous clinical data or approved therapeutic options for this age group. For these reasons, a proportion of pediatricpatients with plaque psoriasis are currently undertreated, and could benefit from additional safe, effective, and convenient therapies. Based on currently available data, guselkumab could offer efficacy, safety and convenience advantages compared with available therapies.

Study objective

Primary Objectives
The primary objective of this study is to evaluate the efficacy and safety of guselkumab in pediatric participants aged >=6 through <18 years with chronic plaque psoriasis.

Secondary Objectives

The secondary objectives of this study are:
• To evaluate the pharmacokinetics (PK) and immunogenicity of guselkumab in pediatric participants aged >=6 through <18 years with chronic plaque psoriasis.
• To evaluate the effect of guselkumab on the dermatologic health-related quality of life in pediatric participants aged >=6 through <18 years with chronic plaque psoriasis.
• To evaluate maintenance of response in participants who have active treatment withdrawn.
• To evaluate the efficacy and safety of retreatment with guselkumab.
• To generate clinical usability data and use experience with the VarioJect presentation (PFS-V) in pediatric participants with chronic plaque psoriasis and a body weight <70 kg.

Study design

This is a Phase 3, multicenter, randomized, placebo- and active comparator-controlled study evaluating the efficacy, safety, and PK of subcutaneously (SC) administered guselkumab for the treatment of chronic plaque psoriasis in pediatric participants >=6 to <18 years of age that cannot be adequately controlled with phototherapy and/or topical agents.
The main study will be conducted in 2 parts. In Part 1, the efficacy, safety, and PK of a weight-based dose regimen of guselkumab will be evaluated in pediatric participants during a 16-week randomized, placebo- and active comparator-controlled period followed by an uncontrolled period of withdrawal and retreatment or initiation of treatment with guselkumab through Week 52. Etanercept (active comparator) will be administered in an open-label fashion during the controlled period of the study and efficacy will be assessed by a blinded efficacy evaluator. Part 1 of the study will be divided into Part 1a (>=12 to <18 years of age [ie, adolescents]) and Part 1b (>=6 to <12 years of age). Enrollment of participants >=6 to <12 years of age in Part 1b will commence only after all participants >=12 to <18 years of age in Part 1a have completed Week 16, all available safety data have been reviewed by an independent Data Monitoring Committee (DMC), with no important safety concerns identified, and all available guselkumab PK data for the >=12 to <18-year-old participants through Week 16 have been evaluated via PK modeling and simulation to confirm that the body weight-based dose used in Part 1a provided systemic exposure comparable to adults.
Part 2 of the study will be an open-label, single-arm study to collect additional efficacy, safety, and PK data for pediatric participants with a weight-based dose regimen of guselkumab through Week 52. Part 2 will begin after the reviews of safety and PK data through Week 16 for all participants >=12 to <18 years of age in Part 1a have been completed, and will enroll enough additional participants to achieve a total of at least 100 participants exposed to guselkumab in this study. Enrollment of participants >=6 to <12 years of age in Part 2 will commence only after all participants in Part 1b have completed

16 weeks of treatment, all available safety data have been reviewed by an independent DMC, and all PK data through Week 16 from Part 1b have been evaluated via PK modeling and simulation to confirm that the body weight-based dose used in Part 1b provided systemic exposure comparable to adults. Clinical usability data of the to-be-marketed VarioJect presentation (PFS-V) will be collected in Part 2 of the study.
A long-term extension (LTE) of the study will be initiated at Week 52.
There are 3 database locks (DBL) planned for this study at Week 16, Week 52 (end of the main study), and at the end of the study (end of the LTE). The Week 16 database lock will occur after all participants in Part 1 of the study complete their Week 16 visit and will include only data from Part 1 of the study. The sponsor will be unblinded after the Week 16 database lock for Part 1 has occurred. The Week 52 database lock will occur after all participants in both Part 1 and Part 2 of the study complete their Week 52 visit. Additional database locks may be performed if deemed necessary.

Intervention

Guselkumab and placebo for guselkumab will be provided in a single-use prefilled syringe (PFS) assembled with the UltraSafe Plus* Passive Needle Guard (PFS-U) or a VarioJect variable dose injector (PFS-V). Commercially available etanercept will be provided in a prefilled syringe or as a powder and solvent for solution for injection.
Participants randomized to guselkumab will receive a dose based on body weight. Participants will receive 1 of the following dose levels depending on their weight:
• Weight <70 kg: 1.3 mg/kg administered using the PFS-V
• Weight >=70 kg: 100 mg administered using the PFS-U
Participants randomized to placebo will receive injections with a volume determined using the same weight based dose calculation for guselkumab.
Commercially available etanercept will be supplied and participants will receive a dose based on body weight:
• <63 kg: 0.8 mg/kg once weekly using a powder and solvent for solution for injection.
• >=63 kg: 50 mg once weekly administered using a prefilled syringe.

Dose Regimen:
Participants in Part 1 will be randomized to 1 of 3 treatment groups to receive:
• Group I: Weight-based guselkumab dose up to 100 mg SC at Weeks 0, 4, and 12.
• Group II: Weight-based placebo for guselkumab dose administered SC at Weeks 0, 4, and 12.
• Group III: Weight-based etanercept dose up to 50 mg SC weekly through Week 15.
From Week 16 through Week 52:
• Group Ia: Participants randomized to guselkumab who are PASI 90 responders at Week 16 will not receive any additional doses of guselkumab until they lose >=50% of their Week 16 PASI response, at which time they will receive a weight-based guselkumab SC dose, followed by a dose 4 weeks later, and every 8

weeks (q8w) thereafter through Week 52.
• Group Ib: Participants randomized to guselkumab who are PASI 90 nonresponders at Week 16 will receive a placebo injection at Week 16 and continue treatment with guselkumab q8w from Week 20 through Week 52.
• Group IIa: Participants randomized to placebo who are PASI 90 responders at Week 16 will not receive any additional doses of study intervention until they lose >=50% of their Week 16 PASI response, at which time they will receive a weight-based guselkumab SC dose, followed by a dose 4 weeks later, and q8w thereafter through Week 52.
• Group IIb: Participants randomized to placebo who are PASI 90 nonresponders at Week 16 will receive a weight-based guselkumab dose at Weeks 16 and 20, followed by q8w dosing thereafter through Week 52.
• Group III: Participants randomized to etanercept who elect to continue in the study will receive a weight-based guselkumab dose at Weeks 20 and 24, followed by q8w dosing thereafter through Week 48.
Participants enrolled in Part 2 of the study will receive a weight-based dose of open-label guselkumab SC at Weeks 0, 4 and q8w thereafter through Week 52.
Participants who complete Week 52 of the main study and who have had a beneficial response from guselkumab treatment as determined by the investigator, will have the option of continuing with a weight-based guselkumab q8w regimen until one of the following occurs: 1) they have reached 18 years of age and reside in a country where guselkumab is approved for treatment of plaque psoriasis in adults and have had the opportunity to complete up to 1 year in the LTE, 2) marketing authorization is obtained for guselkumab for treatment of plaque psoriasis for patients >=6 to <18 years of age, 3) marketing authorization is denied for guselkumab for the treatment of plaque psoriasis in pediatric patients, or 4) the company decides to no longer pursue an indication in plaque psoriasis in the pediatric population.

Study burden and risks

The patient visits the investigator in the part 1 of the study every 4 weeks; in part 2 every 4 or 8 weeks; during the long term extension every 8 weeks. There are multiple blood samples planned. In part 1 and part 2 there are 11 venepunctures. In the long term extension trial there are venipunctures every 24 weeks. A physical examination is performed several times. Questionnaires are taken during all visits.
Side effects of the treatment may occur. These are described in the information for the patient.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Participant must be a boy or girl >=6 to <18 years of age.
2. Have a diagnosis of chronic plaque-type psoriasis for at least 6 months , prior to first administration of study intervention, defined as having at screening and baseline:
• Investigator*s Global Assessment (IGA) >=3 and
• Psoriasis Area and Severity Index (PASI) >=12 and
• >=10% Body Surface Area (BSA) involvement and
at least one of the following:
- very thick lesions or
- clinically relevant facial, genital, or hand/ foot involvement or
- PASI >=20 or
- >20% BSA involvement or
- IGA=4
3. Be a candidate for phototherapy or systemic treatment of plaque psoriasis
4. Have plaque psoriasis considered by the investigator as inadequately controlled with phototherapy and/or topical therapy after an adequate dose and duration of therapy.

5. Be considered, in the opinion of the investigator, a suitable candidate for etanercept (ENBREL) therapy according to their country's approved ENBREL product labeling.
6. Be otherwise healthy on the basis of physical examination, medical history, and vital signs performed at screening. Any abnormalities, must be consistent with the underlying illness in the study population and this determination must be recorded in the participant's source documents and initialed by the investigator.
7. Contraceptive use by boys or girls should be consistent with local regulations regarding the use of contraceptive methods for those participating in clinical studies.
Before randomization, a girl must be either:
a. Not of childbearing potential defined as:
- premenarchal. A premenarchal state is one in which menarche has not yet occurred.
- permanently sterile Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy.
- or otherwise be incapable of pregnancy.
b. Of childbearing potential and practicing a highly effective method of contraception and agrees to remain on a highly effective method while receiving study intervention and until 12 weeks after last dose - the end of relevant systemic exposure.
8. A girl must agree not to donate eggs for the purposes of assisted reproduction during the study and for a period of at least 12 weeks following the last dose of study intervention.
9. A girl of childbearing potential must have a negative urine pregnancy test at screening and at all visits when study intervention is to be administered.
10. A boy who is sexually active with a female of childbearing potential and who has not had a vasectomy must agree to use a barrier method of birth control or a partner with an occlusive cap, during the study and for at least 12 weeks after receiving the last administration of study intervention. All boys must also agree to not donate sperm during the study and for at least 12 weeks after receiving the last administration of study intervention.
11. Are considered eligible according to the following TB screening criteria:
• Have no history of latent or active TB before screening.
• Have no signs or symptoms suggestive of active TB upon medical history and/or physical examination.
• Have had no recent close contact with a person with active TB.

Exclusion criteria

Medical history-related exclusion criteria:
1. Currently has nonplaque forms of psoriasis
2. Has current drug-induced psoriasis

3. Is pregnant, nursing, or planning a pregnancy or fathering a child while enrolled in the study or within 12 weeks after receiving the last administration of study intervention.
4. Has a history of or current signs or symptoms of severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, endocrine, pulmonary, cardiac, neurologic, cerebral, or psychiatric disease.
5. Has a transplanted organ
6. Has had major surgery within 8 weeks before screening, or will not have fully recovered from such surgery, or has such surgery planned during the time the participant is expected to participate in the study.
7. Has unstable suicidal ideation or suicidal behavior:
• Participants >=12 to <18 years of age may not be randomized if they have:
- a Columbia-Suicide Severity Rating Scale rating at screening of: suicidal ideation with intention to act suicidal ideation with specific plan and intent or non-suicidal self-injurious behavior within the past 6 months, OR
- a C-SSRS rating at screening of suicidal behavior
• Participants >=6 to <12 years of age may not be randomized if they have:
- a C-SSRS rating at screening of: suicidal ideation with intention to act suicidal ideation with specific plan and intent r suicidal behavior or any self-injurious behavior ever
• Participants with a C-SSRS rating at screening of Wish to be Dead (*Ideation level 1*), Non-Specific Active Suicidal Thoughts or Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act may not be randomized if:
- participants >=12 to <18 years of age have one of the above C-SSRS ratings within the past 6 months and are determined to be at risk by the investigator after being discussed with the medical monitor or designee.
- participants >=6 to <12 years of age have one of the above C-SSRS ratings ever (lifetime) and are determined to be at risk by the investigator after being discussed with the medical monitor or designee.
8. Is known to have had a substance abuse problem within the previous 12 months.Medical therapies-related exclusion criteria:
9. Has previously received guselkumab or etanercept.
10. Has any contraindications to the use of etanercept per local prescribing information.
11. Criterion modified per Amendment 4:
11.1 Are considered eligible according to the following TB screening criteria:
- have no history of latent or active TB before screening
- have no signs or symptoms suggestive of active TB upon medical history and/or physical examination.
- have had no recent close contact with a person with active TB
- within 10 weeks before the first administration of study intervention, have a negative QuantiFERON-TB Gold test result. Within 10 weeks before the first administration of the study intervention, a negative tuberculin skin test is additionally required if the QuantiFERON-TB gold test is not approved/registered in that country or the tuberculin skin test is mandated by local health authorities.
12. Is not a suitable candidate for anti-TNFα therapy for the following reasons:

• Has a history of known demyelinating diseases such as multiple sclerosis or optic neuritis.
• Has known or suspected intolerance or hypersensitivity to anti-TNFα medications (eg, clinical lupus-like syndrome, serum sickness-like reaction).
• Has a history of, or concurrent congestive heart failure (CHF), including medically controlled CHF.
13. Has received any therapeutic agent directly targeted to IL-12/23, IL-17, or IL-23 within 6 months of the first administration of study intervention (including but not limited to ustekinumab, tildrakizumab, secukinumab, ixekizumab, risankizumab, or brodalumab).
14. Has received natalizumab, efalizumab, or agents that deplete B or T cells within 12 months of screening, or, if after receiving these agents, evidence is available at screening of persistent depletion of the targeted lymphocyte population.Please refer to pages 38-42 of the protocol for the complete overview of the exclusion criteriahat coun

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-03-2019
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Enbrel
Generic name:	Etanercept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tremfya
Generic name:	Guselkumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-06-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-09-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-01-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	07-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-10-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-10-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	17-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-02-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-09-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-02-2023
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	EUCTR2017-003053-42-NL
ClinicalTrials.gov	NCT03451851
CCMO	NL65294.091.18