A Phase 3 Study to Evaluate the Efficacy and Safety of Induction and Maintenance Regimens of Brodalumab Compared With Placebo and Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis: AMAGINE-2

Published: 18-07-2012
Last updated: 26-04-2024

The objective of this clinical research study is to evaluate the safety and effectiveness of brodalumab, compared with ustekinumab and placebo, for the treatment of moderate to severe plaque psoriasis.

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

Summary

ID

NL-OMON41423

Source
ToetsingOnline

Brief title
AMAGINE-2, 20120103

Condition

- Autoimmune disorders

Synonym
Plaque Psoriasis, Psoriasis

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Brodalumab, Head to head, Plaque Psoriasis, Ustekinumab

Outcome measures

Primary outcome

Compared with placebo:

• To evaluate the efficacy of brodalumab (210 mg every 2 weeks [Q2W]; and 140 mg Q2W) in subjects with moderate to severe plaque psoriasis, as measured by the proportion of subjects achieving 75% improvement in Psoriasis Area and Severity Index (PASI; PASI 75) at week 12

• To evaluate the efficacy of brodalumab (210 mg Q2W; and 140 mg Q2W) in subjects with moderate to severe plaque psoriasis, as measured by the proportion of subjects achieving success (clear [0] or almost clear [1]) on the static physician*s global assessment (sPGA) at week 12

Primary Ustekinumab-family Objectives

Compared with ustekinumab:

• To evaluate the efficacy of brodalumab (210 mg Q2W; and 140 mg Q2W for subjects <= 100 kg with 210 mg dosage for subjects > 100 kg) in clearing psoriasis in subjects with moderate to severe plaque psoriasis, as measured by the proportion of subjects achieving PASI 100 at week 12

Secondary outcome

Compared with placebo:

• To evaluate the efficacy of brodalumab (210 mg Q2W; and 140 mg Q2W) in clearing psoriasis, as measured by the proportion of subjects achieving PASI 100 at week 12

• To evaluate the efficacy of brodalumab (210 mg Q2W, and 140 mg Q2W) in clearing psoriasis, as measured by the proportion of subjects achieving sPGA of 0 at week 12

• To evaluate the effect of brodalumab (210 mg Q2W; and 140 mg Q2W) on patient-reported symptoms of psoriasis, as measured by the proportion of subjects who meet the responder definition for the Psoriasis Symptom Inventory (total score <= 8, with no item scores > 1) at week 12

Compared with ustekinumab:

• To evaluate the efficacy of brodalumab (140 mg Q2W) in clearing psoriasis, as measured by the proportion of subjects achieving PASI 100 at week 12

• To evaluate the efficacy of brodalumab (210 mg Q2W; and 140 mg Q2W for subjects <= 100 kg with 210 mg dosage for subjects > 100 kg), as measured by the proportion of subjects achieving PASI 75 at week 12

Maintenance Objectives

• To compare the efficacy of brodalumab maintenance regimens, as measured by the proportion of subjects achieving success on the sPGA at week 52

Safety Objective

• To evaluate the short- (12 week) and long-term (5 year) safety profile of

brodalumab in subjects with moderate to severe plaque psoriasis

Study description

Background summary

Psoriasis is a common inflammatory skin disease occurring in 2% to 3% of the population worldwide (National Psoriasis Foundation website). Moderate to severe plaque psoriasis is, for most patients, a chronic, life-long condition. Currently approved therapies include topical agents (eg, corticosteroids), systemic therapies (eg, methotrexate, cyclosporine, retinoids), phototherapy, and biologics (eg, etanercept, infliximab, adalimumab, ustekinumab) (Hsu et al, 2012; Menter et al, 2008). Many patients nevertheless remain untreated, do not respond to therapy, or suffer from toxicities associated with systemic or phototherapy.

Interleukin (IL)-17 receptor A (IL-17RA) is a type I transmembrane receptor that is found on a wide variety of cell types including epithelial cells, endothelial cells, fibroblasts, chondrocytes, synovial cells, monocytes, neutrophils, and lymphocytes (Yao et al, 1997). IL-17A, IL-17F, IL 17A/F, and IL-25 stimulate cellular responses by interacting with IL-17RA. IL-17A, IL-17F, and IL-17A/F signal via a heteromeric IL-17RA/IL-17RC complex, whereas IL-25 signals via a heteromeric IL-17RA/IL-17RB complex (Rickel et al, 2008; Toy et al, 2006). Brodalumab (AMG 827) is a human anti-IL-17RA monoclonal antibody that selectively targets human IL-17RA and antagonizes the effects of IL-17A, IL-17F, IL-17A/F, and IL-25. Interleukin 17RA blockade represents a novel mechanism.

Study objective

The objective of this clinical research study is to evaluate the safety and effectiveness of brodalumab, compared with ustekinumab and placebo, for the treatment of moderate to severe plaque psoriasis.

Study design

The study consists of a screening period, an induction phase, a maintenance phase, and a long term follow-up period.

After the screening period, this study begins with a 12-week, double-blind,

active comparator- and placebo-controlled induction phase. In this phase, subjects will be randomized in a 2:2:1:1 ratio to receive 210 mg Q2W brodalumab, 140 mg Q2W brodalumab, ustekinumab, or placebo (randomization will be stratified by baseline total body weight (<= 100 kg; > 100 kg), by prior biologic use, and by geographic region; subjects with prior biologic use will be capped at 50% of the study population).

At the week 12 visit
• Subjects originally randomized to either brodalumab arm will be rerandomized (2:2:2:1) into the maintenance phase to receive brodalumab at 210 mg Q2W or 140 mg Q2W, every 4 weeks (Q4W), or every 8 weeks (Q8W). Rerandomization will be stratified by week 12 total body weight (<= 100 kg; > 100 kg), original induction regimen, and week 12 response (sPGA 0 vs sPGA >= 1).
• Subjects originally randomized to ustekinumab will continue to receive ustekinumab.
• Subjects originally randomized to receive placebo will begin receiving 210 mg Q2W brodalumab.

Subjects who do not attend their week 12 visit will not receive any further investigational product (IP).

At week 52, subjects who were originally randomized to ustekinumab will begin receiving 210 mg Q2W brodalumab.

At and after week 16, rescue treatment will be available. The entire study will be up to 271 weeks (approximately 5 years; includes up to 30 days for screening) in duration.

Original and rerandomized treatment assignments will remain blinded until all subjects reach week 52 or terminate the study, whichever comes first.

With protocol amendment #2 Week 266 has been added as safety follow-up visit. The total study duration will now be 271 weeks.

With protocol amendment #3 has been added that starting at the week 64 visit the patient is asked to visit the site every 4 weeks in order to complete two new questionnaires (Columbia Suicide Severity Rating Score and the Patient Health Questionnaire-8).

Intervention

- Completion of subject questionnaires and a subject diary
- Subcutaneous injections with the assigned study medication (brodalumab, ustekinumab, placebo)
- Blood and urine collection
- Additional ECG's
- Photography

- Physical examination
- Chest X-ray (if applicable)

Study burden and risks

Risks: Side effects of the study treatment

Burden:
- Additional visits as described at question E2
- Physical examination
- Blood collection
- Urine collection
- ECG's
- Patient questionnaires
- Completing of a subject diary including adverse events and concomitant medications
- Subcutaneous injections with brodalumab, ustekinumab, and/or placebo
- Optional PK studie
- Photography
- Chest X-ray (if applicable)

Contacts

Public
Amgen

Minervum 7061
Breda 4800 DH
NL
Scientific
Amgen

Minervum 7061
Breda 4800 DH
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subject has had stable moderate to severe plaque psoriasis for at least 6 months before first ose of IP (eg, no morphology changes or significant flares of disease activity in the opinion of the investigator).;Subject must be considered, in the opinion of the investigator, to be a suitable candidate for treatment with a biologic per regional labeling.;Subject has involved body surface area (BSA) >= 10%, PASI >= 12, and sPGA >= 3 at screening and at baseline.;Subject has no known history of active tuberculosis.;Subject has a negative test for tuberculosis during screening

Exclusion criteria

Subject diagnosed with erythrodermic psoriasis, pustular psoriasis, guttate psoriasis, medication-induced psoriasis, or other skin conditions at the time of the screening visit (eg, eczema) that would interfere with evaluations of the effect of IP on psoriasis.;Subject has a planned surgical intervention between baseline and the week 52 evaluation.;Subject has an active infection or history of infections;Subject has any systemic disease considered by the investigator to be clinically significant and uncontrolled.;Subject has known history of Crohn*s disease.;Subject has laboratory abnormalities at screening, including any of the following:
• aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 2x the upper limit of normal
• serum direct bilirubin >= 1.5 mg/dL
• white blood cell (WBC) count < 3.00 x 103/µL
• ANC < 2.00 x 103/µL
• any other laboratory abnormality, which, in the opinion of the investigator, will prevent the subject from completing the study or will interfere with the interpretation of the study results.;Subject has used topical therapy as follows:
• Super-potent or potent topical steroids or topical anthralin/dithranol within 28 days before first dose of IP
• Any other formulation or potency of topical therapy within 14 days before first dose of IP (exception: upper mid-strength or lower potency topical steroids permitted on the face, axillae, and groin; bland emollients [without alpha or beta hydroxy acids]; shampoo without steroids).;Subject has used the following within 28 days of first dose of IP:
ultraviolet A light therapy (with or without psoralen); ultraviolet B light therapy; excimer laser; oral retinoids; methotrexate; cyclosporine; systemically administered calcineurin inhibitors; zathioprine; thioguanine; hydroxyurea; fumarates; or oral or parenteral corticosteroids including intramuscular or intraarticular administration (exception: otic, nasal,

ophthalmic, or inhaled corticosteroids within recommended doses is permitted); other non-biologic systemic therapy for psoriasis.;Subject has received live vaccine(s) within 28 days of the first dose of IP (or longer, according to local requirements for ustekinumab [eg, 1 year in the United States for BCG vaccination]).;Subject has used ustekinumab and/or anti-IL-17 biologic therapy ever or other experimental or commercially available biologic immune modulator(s) within 12 weeks prior to the first IP dose.;Subject currently is enrolled in another investigational device or drug study, or less than 30 days since ending another investigational device or drug study(s), or receiving other investigational agent(s).;For women (except if surgically sterile or at least 2 years postmenopausal, with postmenopausal status confirmed by FSH in the postmenopausal range): not willing to use highly effective methods of birth control during treatment and for 15 weeks after the last dose (if discontinuing before week 52) or for 8 weeks after the last dose (if discontinuing at or after week 52).;For women: pregnant or breast feeding, or planning to become pregnant while enrolled in the study and for 15 weeks after the last dose (if discontinuing before week 52) or for 8 weeks after the last dose (if discontinuing at or after week 52).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-01-2013
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	n.a.
Generic name:	Brodalumab
Product type:	Medicine
Brand name:	Stelara
Generic name:	Ustekinumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-07-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	clinicaltrials.gov, registratienummer n.n.b.
EudraCT	EUCTR2012-000656-34-NL
CCMO	NL40587.018.12