A Multicenter, Randomized, Double-Blind, Secukinumab-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Bimekizumab in Adult Subjects with Moderate to Severe Chronic Plaque Psoriasis

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Primary Objective:The primary objective of this study is to compare the efficacy of bimekizumab administered scfor 16 weeks versus secukinumab at achieving complete clearance (PASI100) in subjects withmoderate to severe chronic plaque PSO.The...

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

Summary

ID

NL-OMON55812

Source
ToetsingOnline

Brief title
UCB - PS0015

Condition

- Autoimmune disorders
- Epidermal and dermal conditions

Synonym
Psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: UCB Pharma
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Bimekizumab Secukinumab, Efficacy Safety, Phase 3b, Psoriasis

Outcome measures

Primary outcome

The primary efficacy variable is the PASI100 response, defined as complete

clearance from Baseline in the PASI score, at Week 16.

Secondary outcome

The secondary efficacy variables are:

* PASI75 response at Week 4

* PASI90 response at Week 16

* PASI100 response at Week 48

* IGA response (0/1) at Week 16

The secondary safety variables are:

* TEAEs adjusted by duration of subject exposure to IMP

* SAEs adjusted by duration of subject exposure to IMP

* TEAEs leading to withdrawal adjusted by duration of subject exposure to study

treatment

Other efficacy variables: The other efficacy variables are listed below and

will be evaluated according to the planned assessments (see protocol Table 5*

1). This excludes the time points for the primary and secondary variables

specified above in protocol Section 4.1 and Section 4.2.1, respectively.

The other efficacy variables are:

* PASI75, PASI90, and PASI100 response

* Time to PASI75, PASI90, and PASI100 response

* Absolute and percent change from Baseline in PASI

* Percentage of subjects with PASI *1, *2, *3, and *5

* IGA response (Clear)

* IGA response (Clear or Almost Clear with at least 2 category improvement

relative to

* Baseline)

* Shift from Baseline in IGA score

* Absolute and percent change from Baseline in the BSA affected by PSO

* Change from Baseline in Dermatology Life Quality Index (DLQI)

* Percent of subjects achieving a DLQI total score of 0 or 1

* Percent of subjects achieving a minimal clinically important difference

(improvement from Baseline of 4 or more) in the DLQI

* Change from Baseline in the Patient's Global Assessment of Disease Activity

(PGADA) for the arthritis visual analog scale (VAS) in subjects with PsA at

Baseline

* Change from Baseline in Patient Global Assessment of PSO score

* Change from Baseline in symptoms of PSO (itch, pain, and scaling)

* Change from Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) score

for subjects with nail PSO at Baseline

* Scalp-specific Investigator*s Global Assessment (scalp IGA) response (0/1 and 0) at Week 16 for subjects with scalp PSO at Baseline

* Scalp IGA response (0/1 and 0) for subjects with scalp PSO at Baseline

* Palmoplantar Investigator*s Global Assessment (pp-IGA) response (0/1 and 0) for subjects with palmoplantar PSO at Baseline

* Responses to the European Quality-of-Life 5-Dimensions 3-Level (EQ-5D-3L) dimensions, absolute and changes from Baseline in EQ-5D-3L VAS scores

* Change from Baseline in Work Productivity and Activity Impairment Questionnaire-specific health problem (WPAI-SHP) V2.0 adapted to PSO scores

* Change from Baseline in the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire scores (function score, symptom score, and total score)

Other safety variables to be assessed are:

* Severity and frequency of AEs

* Change from Baseline in vital signs

* ECG results

* Change from Baseline in clinical laboratory values (chemistry, hematology, and urinalysis)

* Change from Baseline in Patient Health Questionnaire-9 (PHQ-9) scores

Physical examination findings considered clinically significant changes since the physical examination at the Screening Visit will be recorded as AEs.

The Pharmacokinetic variable is the plasma concentration of bimekizumab.

The immunological variable is the anti-bimekizumab antibody level prior to and

following IMP administration.

Study description

Background summary

Psoriasis is a common, chronic inflammatory disease characterized by a series of linked cellular changes in the skin: hyperplasia of epidermal keratinocytes, vascular hyperplasia and ectasia, and infiltration of T-lymphocytes, neutrophils, and other types of leukocytes in affected skin. Though the pathophysiology of PSO is not fully understood, the importance of T-cells and inflammatory cytokines has been demonstrated by the clinical benefit provided by therapies directed at these targets (Krueger and Ellis, 2005).

There are a variety of forms of PSO including plaque, guttate, inverse, pustular, and erythrodermic. Plaque PSO is the most common, comprising approximately 80% to 90% of all cases. Approximately 17% of those with PSO have moderate to severe disease (Kurd et al, 2008).

In addition to the impact on skin, PSO has a multitude of psychosocial and emotional effects on patients, including increased self-consciousness, frustration, fatigue, depression, and suicidal ideation. As a result, patients frequently report sleeping problems, difficulties at work, problems interacting with family members, disrupted leisure activities, and sexual difficulties (Dowlatshahi et al, 2014; Gottlieb, 2005; Mukhtar et al, 2004; Ortonne, 2004; Krueger et al, 2001).

A number of comorbidities have been associated with PSO, especially with more severe PSO. Psoriatic arthritis (PsA), cardiovascular disease, metabolic syndrome, chronic pulmonary disease, peptic ulcer disease, renal disease, and diabetes have all been demonstrated to have an increased prevalence in PSO patients (Yeung et al, 2013; Christophers et al, 2010; Gisondi et al, 2007; Gelfand et al, 2006).

Study objective

Primary Objective:
The primary objective of this study is to compare the efficacy of bimekizumab administered sc
for 16 weeks versus secukinumab at achieving complete clearance (PASI100) in subjects with
moderate to severe chronic plaque PSO.

The secondary objectives of the study are to:
* Evaluate the efficacy of bimekizumab compared with secukinumab after 4 weeks, 16 weeks, and 48 weeks of treatment.
* Assess TEAEs, SAEs, and TEAEs leading to withdrawal adjusted by duration of subject exposure to IMP.

The other objectives of the study are to demonstrate the effects of bimekizumab on the following aspects of the disease:
* Assess the efficacy of bimekizumab over time
* Assess the change of skin-related quality of life (QOL)
* Assess the change of general health-related QOL
* Assess the change in nail PSO over time in subjects with nail PSO at Baseline
* Assess the change in psoriatic scalp disease over time in subjects with scalp PSO at Baseline
* Assess the change in psoriatic palmoplantar disease over time in subjects with palmoplantar
* PSO at Baseline
* Assess the change in patient global assessment PSO score
* Assess the change in symptoms of PSO (itch, pain, and scaling) as reported by subjects
* Assess work productivity status
* Assess the safety and tolerability of bimekizumab
* Assess the PK of bimekizumab
* Assess the immunogenicity of bimekizumab

Study design

This is a Phase 3b, multicenter, randomized, double-blind, active comparator-controlled, parallel-group study to evaluate the efficacy and safety of bimekizumab compared with secukinumab in adult subjects with moderate to severe chronic plaque psoriasis (PSO).
For each subject, the study will last a maximum of 69 weeks and will consist of 3 periods, a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at 44 weeks), and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]).
During the Treatment Period, eligible subjects will be randomized 1:1 to receive one of the
following blinded IMP regimens:
* Bimekizumab 320mg administered subcutaneously (sc) every 4 weeks (Q4W)
* Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W
Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.
Investigational medicinal product will be administered at Baseline, Weeks 1, 2, 3, and 4 and then Q4W thereafter, until Week 16. At week 16 subjects in the bimekizumab treatment group will be reassigned to receive one of the following treatment options;

* Bimekizumab 320 mg subcutaneous (sc) administered every 4 weeks (Q4W)
* Bimekizumab 320 mg subcutaneous (sc) administered every 8 weeks (Q8W) and placebo in weeks 20, 28, 36 and 44.

All doses will be administered in the clinic.
At Week 48, all subjects will undergo the Week 48 study assessments and will enter the SFU Period.
Subjects withdrawing early from the study will undergo the Premature End of Treatment (PEOT) Visit assessments and will enter the SFU Period.

Intervention

Depending on the treatment arm, subjects will be administered:
- Bimekizumab 320 mg sc at baseline and thereafter every 4 weeks. In weeks 1, 2 and 3 they will be administered placebo sc to maintain the blind.
- Secukinumab 300 mg sc at baseline, weeks 1, 2, 3 and thereafter every 4 weeks.

Subjects in the Bimekizumab treatment group will be reassigned at week 16 to receive bimekizumab every 4 weeks or every 8 weeks. Subject who will receive bimekizumab every 8 weeks will receive a placebo in the other weeks to maintain blinding.

Study centers and number of patients planned:
Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. There will be approximately 350 subjects in the bimekizumab 320mg treatment arm and 350 subjects in the secukinumab 300mg treatment arm. The planned number of study sites is approximately 86. Every eligible subject who signs an ICF will be randomized.

The regions planned for study conduct are North America, Western Europe, and Central/Eastern Europe, with possible extension to other regions and countries.

Study burden and risks

The study burden consists of:
- Visits to the study doctor: 18 visits
- Blood draws: 13 times
- Urine screenings: 8 times
- Sc injections: 30 injections
- Chest X-ray: 1 (at screening visit)
- ECGs: 4 times
- Physical exam: 6 times
- Questionnaires: on mental health status, quality of life, status of disease

activity and skin pain level

The patient may experience physical or psychological discomfort from the above tests, procedures and questionnaires.

The patient may also experience side effects from the study medication.

Contacts

Public
UCB Pharma

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Scientific
UCB Pharma

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male or female at least 18 years of age, - Subject must have had chronic plaque psoriasis (PSO) for at least 6 months prior to the Screening visit, - Subject must have Psoriasis Area Severity Index (PASI) ><=12 and body surface area (BSA) affected by PSO ><=10% and Investigator*s Global Assessment (IGA)

score ><=3 on a 5 point scale, - Subject must be a candidate for systemic PSO therapy and/or phototherapy, - Subject must be considered, in the opinion of the Investigator, to be a suitable candidate for treatment with secukinumab per regional labeling and has no contraindications to receive secukinumab as per the local label, - Female subject of child bearing potential must be willing to use highly effective method of contraception

Exclusion criteria

- Subject has an active infection (except common cold), a serious infection, or a history of opportunistic, recurrent or chronic infections, - Subject has concurrent acute or chronic viral hepatitis B or C or human immunodeficiency virus (HIV) infection, - Subject has known tuberculosis (TB) infection, is at high risk of acquiring TB infection, or has current or history of nontuberculous mycobacterium (NTMB) infection, - Subject has any other condition, including medical or psychiatric, which, in the Investigator's judgment, would make the subject unsuitable for inclusion in the study, - Presence of active suicidal ideation or severe depression, - Subject has any active malignancy or history of malignancy within 5 years prior to the Screening Visit EXCEPT treated and considered cured cutaneous squamous or basal cell carcinoma, or in situ cervical cancer

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2019

Enrollment:	21
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bimekizumab
Generic name:	Bimekizumab
Product type:	Medicine
Brand name:	Secukinumab
Generic name:	Cosentyx
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-07-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	26-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	14-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2022
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
EudraCT	EUCTR2017-003784-35-NL
ClinicalTrials.gov	NCT03536884
CCMO	NL66095.018.18