A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study Evaluating the Efficacy and Safety of Bimekizumab in Study Participants With Moderate to Severe Hidradenitis Suppurativa

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The purpose of this study is to find out how safe and effective a new drug called bimekizumab is for long-term use in treating hidradenitis suppurativa. Bimekizumab (hereafter referred to as *the study drug*) has been approved by the health...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Interventional

Summary

ID

NL-OMON52878

Source
ToetsingOnline

Brief title
BE HEARD I

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
Acne inversa / acne ectopica

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Bimekizumab, Efficacy and Safety, Hidradenitis Suppurativa, Phase 3

Outcome measures

Primary outcome

Evaluate the efficacy of bimekizumab in study participants with moderate to

severe HS

- HiSCR50 at Week 16

Secondary outcome

Evaluate the efficacy of bimekizumab on other measures of disease activity in

study participants with moderate to severe HS

• HiSCR75 at Week 16

• Flare (defined as a >=25% increase in AN count with an

absolute increase in AN count of >=2 relative to Baseline) by Week 16

• Absolute change from Baseline in DLQI Total Score at

Week 16

• Absolute change from Baseline in the Worst HS Skin Pain

score at Week 16, as assessed by the *worst pain* item

(11-point numeric rating scale) in the HSSDD

• Pain response (defined as a decrease from Baseline in

HSSDD weekly worst skin pain score at or beyond the threshold for clinically

meaningful change) at Week 16

Evaluate the safety of bimekizumab in study participants with moderate to

severe HS

- Treatment-emergent AEs

- Serious TEAEs

- TEAEs leading to withdrawal from study

Study description

Background summary

Hidradenitis suppurativa or acne inversa is a chronic, inflammatory, recurrent, debilitating skin disease that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillaries, inguinal, and anogenital regions (Dessau definition, First International Conference on HS, 30 Mar to 01 Apr 2006, Dessau, Germany). The nodules are often inflamed, can progress to abscess formation, and may rupture to form fistulas and subsequent scarring. Thus, many patients with HS develop permanent sequelae of past inflammation that are only remediable through surgical excision of the involved skin areas. Hidradenitis suppurativa is also associated with several complications (eg, the development of anal, urethral, and rectal strictures and fistulas), and the excessive scarring and fibrosis produced by HS lesions can lead to contractures and limitations in limb mobility (Alikhan, 2009; Danby, 2010).
Hidradenitis suppurativa is estimated to affect about 1% of the adult European population, with a female to male ratio of approximately 3:1 (Revuz, 2008; Naldi, 2006). The prevalence of diagnosed HS in the US may be lower (<0.1%), although further research is needed to determine the prevalence of undiagnosed HS in the US (McMillan, 2014). Patients diagnosed with HS often experience a significant reduction in quality of life (QOL), equivalent to severe PSO (Sartorius, 2009), due to the location of, and discharge from, the lesions that leads to an often persistent morbidity due to pain and sequelae from uncontrolled inflammation (von der Werth, 2001; Wolkenstein, 2007). The reduction in QOL and persistent morbidity result in functional impairment in patients with HS similar or greater to that of heart disease, diabetes, or asthma, when measured by the European Quality-of-Life 5 dimensions 3-level questionnaire (EQ-5D-3L) scale (Riis, 2016).

Bimekizumab is a humanized full-length mAb of IgG1 subclass being developed for the treatment of patients with inflammatory diseases such as PSO, psoriatic arthritis, axial spondyloarthritis, and HS. Bimekizumab has high affinity for human IL-17A and human IL-17F,
and selectively and potently inhibits the activity of both isoforms in vitro.
The key pro-inflammatory cytokine IL-17A has been demonstrated to, and IL-17F is believed to, play important roles in autoimmune and inflammatory diseases. Published data and immunohistochemistry studies performed by UCB have shown that expression of both IL-17A and IL-17F is present in HS lesions, and there are published reports highlighting the potential for IL-17A and IL-17F to drive HS disease pathology (UCB Research Report 40001864; Cho, 2012; Schlapbach, 2011). This supports the hypothesis that the IL-17 cytokine family is a potential therapeutic target in HS. Bimekizumab is hypothesized to demonstrate a treatment response in HS because it selectively and potently inhibits the activity of both IL-17A and IL-17F isoforms in vitro.

Study objective

The purpose of this study is to find out how safe and effective a new drug called bimekizumab is for long-term use in treating hidradenitis suppurativa. Bimekizumab (hereafter referred to as *the study drug*) has been approved by the health authorities for treatment of moderate to severe plaque psoriasis in adults in the European Union and Great Britain. However, it is still investigational, which means that is it still being tested, and has not yet been approved for treatment by the health authorities in other countries or regions or in other indications.
We compare the effects of the study drug with the effects of a placebo. A placebo is a substance without active substance, a *fake drug*.

Study design

HS0003 is a Phase 3, randomized, double-blind, placebo-controlled, multicenter, pivotal study evaluating the efficacy and safety of bimekizumab in study participants with moderate to severe HS. Study participants meeting the inclusion criteria who do not meet any exclusion criteria will complete a Screening Period of 14 days to up to 5 weeks; a double-blind, 48-week Treatment Period comprising a 16-week Initial Treatment Period and 32-week Maintenance Treatment Period; and a 20-week Safety Follow-up (SFU) Period following the final injection of investigational medicinal product (IMP) if study participants do not enter a subsequent extension study (HS0005) or withdraw prematurely from treatment.
Study participants will be randomized in a 2:2:2:1 ratio (stratified by Hurley Stage and current antibiotic use) to 1 of 3 dose regimens of bimekizumab or placebo as shown in the schematic (Figure 1-1). All doses of IMP will be administered by sc injection. The primary efficacy variable at Week 16 is HiSCR50. Study visits will occur at Screening; Baseline

(Week 0); Weeks 1, 2, 4, 6, 8, 10, 12, 14, and 16; and every 2 weeks from Week 16 through
Week 48 for assessments of efficacy, safety, and other measures of QOL/health status/work productivity. An SFU visit will be conducted 20 weeks after the final dose of IMP for participants who do not enter the extension study, or who are prematurely withdrawn from the study.

Intervention

Because of differences in the dosing schedules and in order to maintain blinding, all study participants will receive 2 injections subcutaneous every 2 weeks from Week 0 to Week 46 as depicted in Table 6*2 (protocol).

Bimekizumab will be administrated via a subcutaneous injection.
Eligible study participants will be randomized in a 2:2:2:1 ratio as noted in the Study Schema

Participants who will only receive Bimekizumab they will receive 320mg every two weeks. This will be given with two injections of 160 mg.

There are also 3 groups who will receive both Bimekizumab and a Placebo. Please see Protocol amendment 2 for a schematic table 6-2 (page 35)

Study burden and risks

At the Baseline visit, the subject will be randomly assigned (like drawing straws) to receive either the study drug or a placebo for the first 16 weeks. Neither the subject nor the study doctor will know which treatment the subjects are receiving, this is called *double blind*. The subject will have a 6 in 7 chance of receiving the active study drug and a 1 in 7 chance of receiving placebo only for the first 16 weeks of treatment. After 16 weeks, all subjects will receive the active study drug for the remaining 32 weeks of the study. Each injection will be given under the skin either on the lower stomach area, upper arm, or the outer side of the upper thighs. The place of injection will be rotated between visits. The subject will receive two injections of the assigned study drug every two weeks during the treatment period.

Assessments done as screening may be repeated, additional procedures include:
• Recording height and weight.
• Check if the subjects are still eligible to take part in the study and decide if the subject may continue in the study.
• Questions about any health problems including tobacco and alcohol use or other medical conditions that the subject may have had since the last visit.
• Questions about other medications the subjects are taking during the study. the subject will also be asked if the subject started, stopped, or modified any medications since your last visit and this will be recorded by the subjects

study doctor.
• The subject will be asked to complete a daily diary, at the end of every day, from the start of Screening through the Week 16 visit to assess their symptoms for the past 24-hours.
• The subject will be asked to give their assessment on the status of your hidradenitis suppurativa and score the severity of their skin pain at up to 5 visits (Baseline, Weeks 4, 16, 32, and 48 visits).
• Additional questionnaires about;
- symptoms of hidradenitis suppurativa the subject have experienced in past 7 days.
- how their disease affects their quality of life.
- how their disease affects their work efficiency.

Extension Study
At the completion of 48 weeks of Treatment Period, if there is any improvement in their condition as determined by the study doctor, the subject will be given an option to participate in an extension study.

Safety Follow-Up / Premature End of Treatment Visit
If the subject do not qualify for, or do not want to participate in the extension study, the subject will return for a Safety Follow-up visit 20 weeks after their final dose of study drug.
A Premature End of Treatment visit will be performed if the subject leave the study early before the study completion at Week 48, either because the subject decided to discontinue by theirself, or because of safety issues regarding their personal health as determined by their study doctor. Most of the assessments performed during the Treatment Period visits will be repeated during this visit.
If the subject stop receiving the study drug, the subject will still be a part of the study. The subject will be asked to complete the Premature End of Treatment visit assessments and return to the clinic for an SFU visit at 20 weeks after their final dose of study drug.

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

- Participant must be at least 18 years of age, at the time of signing the informed consent. If a study participant is under the local age of consent and is at least 18 years of age, written informed consent will be obtained from both the study participant and the legal representative
- Study participants must have a diagnosis of Hidradenitis Suppurativa (HS) based on clinical history and physical examination for at least 6 months prior to the Baseline visit; diagnosis must be verifiable through medical notes and documentation.
- Study participant must have HS lesions present in at least 2 distinct anatomic areas (eg, left and right axilla), 1 of which must be at least Hurley Stage II or Hurley Stage III at both the Screening and Baseline visits
- Study participant must have moderate to severe HS defined as a total of >=5 inflammatory lesions (ie, number of abscesses plus number of inflammatory nodules) at both the Screening and Baseline visits
- Study participant must have had a history of inadequate response to a course of a systemic antibiotics at the Screening Visit for treatment of HS as assessed by the Investigator through study participant interview and review of medical history; inadequate response must be verifiable through medical notes and documentation.
- A female study participant is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies:
a) Not a woman of childbearing potential (WOCBP)
OR
b) A WOCBP who agrees to follow the contraceptive guidance during the treatment

period and for at least 20 weeks after the last dose of investigational medicinal product (IMP)

Exclusion criteria

1. Study participant has any medical or psychiatric condition that, in the opinion of the
Investigator, could jeopardize or would compromise the study participant*s ability to participate in this study as determined by the Investigator based on protocol-required assessments.
2. Study participant has a draining tunnel count of >20 at the Baseline Visit.
3. Study participant has any other active skin disease or condition (eg, bacterial cellulitis,
candida intertrigo, extensive condyloma) that may, in the opinion of the Investigator, interfere with the assessment of HS.
4. Study participant has a diagnosis of sarcoidosis, systemic lupus erythematosus, or active
IBD. Note: Study participants with a diagnosis of Crohn*s disease or ulcerative colitis are allowed if they have no active symptomatic disease at Screening or Baseline.
5. Study participant has a primary immunosuppressive condition, including taking immunosuppressive therapy following an organ transplant, or has had a splenectomy.
6. Female study participant who is breastfeeding, pregnant, or plans to become pregnant during
the study or within 20 weeks following the final dose of IMP.
7. Study participant has an active infection or history of infection(s) as follows:
* Any infection requiring systemic treatment within 14 days prior to Baseline
* A serious infection, defined as requiring hospitalization or intravenous anti-infective(s)
within 2 months prior to the Baseline Visit
A history of opportunistic, recurrent, or chronic infections that, in the opinion of the
Investigator, might cause this study to be detrimental to the study participant. Opportunistic infections are infections caused by uncommon pathogens (eg, Pneumocystis jirovicii, cryptococcosis), or unusually severe infections caused by common pathogens (eg, cytomegalovirus, herpes zoster)
8. Study participant has any of the following:
* Known active TB disease
* History of active TB involving any organ system unless adequately treated according to
World Health Organization/Centers for Disease Control and Prevention therapeutic guidance and proven to be fully recovered upon consult with a TB specialist

* Latent TB infection (LTBI). Participants with LTBI diagnosed during Screening must
have completed a course of prophylaxis prior to IMP dosing. Participants can be rescreened after completion of a full course of prophylaxis plus a wash-out of least
5 half-lives of the prophylactic medication(s) prior to Baseline to avoid any interference
with the study efficacy measurements (eg, concomitant antibiotics). Prophylaxis should be in accordance with applicable clinical guidelines and TB specialist judgment based on the origin of infection.
* High risk of exposure to TB infection
* Current pulmonary nontuberculous mycobacterial (NTM) infection or history of pulmonary NTM infection unless proven to be fully recovered
Note: For further information relating to definitions of known active TB, past history of TB, LTBI, high risk of acquiring TB infection and NTM infection refer to Section 8.2.6.
9. Study participant has an acute or chronic hepatitis B virus, hepatitis C virus (HCV), or
human immunodeficiency virus (HIV) infection. Study participants who have evidence of, or tested positive for, hepatitis B or hepatitis C will be excluded. A positive test for hepatitis B virus is defined as: 1) positive for hepatitis B surface antigen, or 2) positive for anti-hepatitis B core antibody. A positive test for HCV is defined as: 1) positive for hepatitis C antibody, and 2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction).
10. Study participants with concurrent malignancy are excluded. Study participants with a
history of malignancy within the past 5 years prior to the Screening Visit are excluded, EXCEPT if the malignancy was a cutaneous squamous or basal cell carcinoma, or in situ cervical cancer that has been treated and is considered cured.
11. Study participant has a history of a lymphoproliferative disorder including lymphoma or
current signs and symptoms suggestive of lymphoproliferative disease.
12. Study participant has had major surgery within the 3 months prior to the Baseline Visit, or
has planned major surgery after entering the study.
13. Study participant has any systemic disease (ie, cardiovascular, neurological, renal, liver,
metabolic, gastrointestinal, hematological, immunological, etc.) considered by the degree during the course of the study.
14. Study participant has had a myocardial infarction or stroke within the 6 months prior to the
Screening Visit.
15. Study participant has a history of chronic alcohol or drug abuse within 6 months prior to
Screening as evaluated by the Investigator based on medical history, interview,

and/or results of the Screening urine drug screen.
16. Study participant has the presence of active suicidal ideation, or positive suicide behavior using the "Screening" version of the electronic Columbia Suicide Severity Rating Scale (eC-SSRS) with either of the following criteria:
* Study participant has a history of a suicide attempt within the 5 years prior to the
Screening Visit. Study participants with a history of a suicide attempt more than 5 years ago should be evaluated by a mental healthcare practitioner before enrolling into the study.
* Suicidal ideation in the past month prior to the Screening Visit as indicated by a positive
response (*Yes*) to either Question 4 or Question 5 of the *Screening* version of the
eC-SSRS.
17. Study participant has presence of moderately severe major depression or severe major
depression indicated by a score of >=15 using the screening Patient Health Questionnaire Depression Module (PHQ-9). Medication used to treat depression should be stable for
8 weeks prior to Baseline.
18. Study participant has a known hypersensitivity to any components of bimekizumab or
comparative drugs as stated in this protocol.
19. Study participant has had prior treatment with an IL-17 biologic response modifier or
has participated in IL-17 biologic response modifier study unless an appropriate washout has been performed since the last dose of IMP (within 6 moths prior to the Baseline Visit or 5 hal-lives [whichever is greater]).
20. Study participant received prescription topical therapies for the treatment of HS within
14 days prior to the Baseline Visit.
21. Study participant is currently receiving systemic nonbiologic or biologic therapies for HS
with potential therapeutic impact for HS. Note: If study participant received systemic nonbiologic or biologic therapies for HS and stopped these treatments, washout periods should be applied as shown in Table 6*3. Note: this does not apply to study participants who may be eligible for randomization into the antibiotic strata.
22. If study participant is using concomitant, non-opioid analgesics for HS-related or
non-HS-related pain as permitted by protocol, they should be on a stable (scheduled) dose for at least 14 days prior to the Baseline Visit and anticipate continuing that dose through
Week 16 unless a decrease in dose is warranted based on symptoms. Opioid analgesics are
excluded. Note: As needed (PRN) use is not considered a stable dose, but (for example) taking a nonsteroidal anti-inflammatory drug (NSAID) 3 times per week,

every week is considered a stable dose.
23. Study participant has received any live (including attenuated) vaccination within the 8 weeks
prior to the Baseline Visit (eg, inactivated influenza and pneumococcal vaccines are allowed, but nasal influenza vaccination is not permitted). Live vaccines are not allowed during the study, including the SFU Period (20 weeks after the final dose of IMP).
24. Study participant has received Bacillus Calmette-Guerin vaccination within 1 year prior to
IMP administration.
Prior/Concurrent clinical study experience
25. Study participant has previously participated in this study or study participant has previously
been assigned to treatment in a study of the medication under investigation in this study, and received at least 1 dose of IMP (including placebo).
26. Study participant is currently participating in another study of a systemic medication under
investigation, including SFU. Study participant must be washed out of the medication as indicated in Table 6*3.
27. Study participant is currently participating in another study of a topical medication under
investigation, including SFU. Study participant must be washed out of the medication for 4 weeks prior to the Baseline Visit.
28. Study participant is currently, or was within the 4 weeks prior to the Baseline Visit,
participating in another study of a medical device under investigation.
Diagnostic assessments
29. Study participant has laboratory abnormalities at Screening, including any of the following:
* >=3× the upper limit of normal (ULN) of any of the following: alanine aminotransferase
(ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP)
* Bilirubin >1.5×ULN (isolated bilirubin >1.5×ULN is acceptable if bilirubin is fractionated and direct bilirubin <35%)
* White blood cell count <3.00×103/µL
* Absolute neutrophil count <1.5×103/µL
* Lymphocyte count <500 cells/µL
* Hemoglobin <8.5g/dL
Note: Individual screening tests for which the results are in error, borderline, or indeterminate for inclusion in the study can be repeated once for confirmation during the Screening Period. Upon retesting, study participants whose results remain outside this threshold should not be randomized.
30. Study participant has any other laboratory abnormality, which, in the opinion of the
Investigator, will prevent the study participant from completing the study or will interfere with the interpretation of the study results.

Other exclusions
31. Study participant is a UCB employee or is an employee of third-party organizations involved
in the study.
32. Study participant and/or his or her immediate family member is an employee, volunteer, or
other worker at the investigative site either affiliated or not affiliated with this study. Immediate family is defined as a spouse, parent, child, or sibling whether biological or legally adopted.

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:	Recruitment stopped
Start date (anticipated):	02-03-2021
Enrollment:	27
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bimekizumab
Generic name:	Bimekizumab

Ethics review

Approved WMO Date:	25-03-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-10-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-08-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	31-01-2023
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	EUCTR2019-002550-23-NL
ClinicalTrials.gov	NCT04242446
CCMO	NL72332.078.20