A Phase 2 Multicenter, Investigator-blind, Subject-blind, Placebo-controlled Study of the Efficacy, Safety, and Pharmacokinetics of Bimekizumab in Subjects with Moderate to Severe Hidradenitis Suppurativa

Published: 31-10-2017
Last updated: 12-04-2024

Primary objectiveThe primary objective of this study is to evaluate the efficacy of bimekizumab in subjects with moderate to severe HS.Secondary objectiveThe secondary objective of this study is to assess the safety, tolerability, immunogenicity,...

Ethical review	Not approved
Status	Will not start
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON44288

Source
ToetsingOnline

Brief title
HS0001

Condition

- Epidermal and dermal conditions

Synonym
acne inversa

Research involving

Human

Sponsors and support

Primary sponsor: UCB Pharma
Source(s) of monetary or material Support: de sponsor UCB.

Intervention

Keyword: Bimekizumab, Hidradenitis Suppurativa, Phase 2 study, Placebo-controlled Study

Outcome measures

Primary outcome

Primary End Point

Percentage of subjects achieving clinical response as measured by Hidradenitis

Suppurativa Clinical Response (HiSCR).

Timepoint(s) of evaluation of this end point: Baseline, Week 12

Secondary outcome

Secondary End Point

1. Bimekizumab plasma concentration at Visit 2

2. Bimekizumab plasma concentration at Visit 3

3. Bimekizumab plasma concentration at Visit 4

4. Bimekizumab plasma concentration at Visit 8

5. Bimekizumab plasma concentration at Visit 11

6. Bimekizumab plasma concentration at Visit 12

7. Number of Adverse Events (AE)

8. Number of Adverse Events categorized by severity

9. Number of Serious Adverse Events (SAEs)

10. Number of Serious Adverse Events (SAEs) categorized by severity

11. Number of subjects withdrawing due to Adverse Events

12. Change from Baseline in vital signs (blood pressure [BP] and pulse rate) and body weight

13. Change from Baseline in ECG parameters

14. Change from Baseline in clinical laboratory parameters (hematology, biochemistry, and urinalysis)

15. Change from Baseline in physical examination

16. Bimekizumab Anti-Drug Antibody (ADA) concentration at Visit 2

17. Bimekizumab Anti-Drug Antibody (ADA) concentration at Visit 3

18. Bimekizumab Anti-Drug Antibody (ADA) concentration at Visit 4

19. Bimekizumab Anti-Drug Antibody (ADA) concentration at Visit 8

20. Bimekizumab Anti-Drug Antibody (ADA) concentration at Visit 11

21. Bimekizumab Anti-Drug Antibody (ADA) concentration at Visit 12

Timepoint(s) of evaluation of this end point

1,16. Visit 2 (Day 1)

2,17. Visit 3 (Week 2)

3,18. Visit 4 (Week 4)

4,19. Visit 8 (Week 8)

5,20. Visit 11 (Week 12)

6,21. Visit 12 (Week 30)

Study description

Background summary

Hidradenitis suppurativa is difficult and challenging to treat. Treatment depends on the stage of disease (eg, presence of inflammatory components and/or scarring). Most patients respond only partially to treatment, or the disease rapidly reoccurs after drug cessation. Historically, available treatment options for HS varied widely and with the exception of the recent European and German treatment guidelines, there were few formal treatment guidelines for this condition (Zouboulis et al, 2015b). Bacterial infection is believed to be a secondary event in the disease process (Nikolakis et al, 2015; Nikolakis et al, 2016). While antibiotics generally do not cure the disease, they may relieve symptoms through either an antibacterial or an anti inflammatory effect. Topical antimicrobials are generally given for mild disease (either topical antiseptics, such as chlorhexidine, or topical antibiotics, such as clindamycin), with modest results (Clemmensen, 1983). Further treatment of HS can depend on the extent and activity of the disease and include medical treatments (eg, systemic combination therapy with clindamycin and rifampicin, tetracyclines including doxycycline and minocycline, intralesional triamcinolone, systemic cyclosporine, anti androgen treatment in women, systemic dapsone, systemic retinoids, and metformin), surgical treatments (eg, radical excision, marsupialization, and deroofing), and laser treatment (Naldi, 2006; Jemec, 2010; Zouboulis et al, 2015b).
Adalimumab is the only approved medicinal product for the treatment of moderate to severe HS with an inadequate response to conventional systemic HS therapy (approved in Sep 2015). However, 2 randomized, double-blind, placebo controlled studies of adalimumab in a total of 633 adult subjects with moderate to severe HS indicated that only around 50% of subjects achieved a clinical response at Week 12. During the second part of both studies (up to 36 week treatment duration), approximately 40% of subjects who initially responded to adalimumab weekly therapy continued to benefit from this drug (Kimball et al, 2016a).
In summary, there is still a significant unmet medical need for additional therapies to treat this condition. In addition, given the significant reduction in QOL and functional impairment experienced by patients diagnosed with HS, there is an unmet need for medical therapies that can have a substantial impact on improving a patient*s QOL.

Study objective

Primary objective

The primary objective of this study is to evaluate the efficacy of bimekizumab in subjects with moderate to severe HS.

Secondary objective

The secondary objective of this study is to assess the safety, tolerability, immunogenicity, and PK of bimekizumab in subjects with moderate to severe HS.

Study design

Study description

HS0001 is a Phase 2 multicenter, randomized, Investigator-blind, subject-blind, placebo controlled, active reference arm study to assess the efficacy, safety, and PK of bimekizumab in eligible adult subjects with moderate to severe HS. To be eligible to participate in this study, subjects must be adults with a diagnosis of moderate to severe HS for at least 1 year prior to Screening (lesions present in at least 2 distinct anatomic areas [1 of which must be at least Hurley Stage II or III] and a total abscess and inflammatory nodule count *3) that has been stable for at least 2 months prior to Screening with an inadequate response to at least a 3-month study of an oral antibiotic treatment for HS (or exhibited recurrence after discontinuation to, or demonstrated intolerance to, or have a contraindication to oral antibiotics for treatment of their HS).

Study periods

This study will include 3 periods: a Screening Period (*2 weeks up to a maximum of 4 weeks prior to randomization), a Treatment Period (12 weeks), and a SFU Period (20 weeks after the last dose of IMP).

Study duration per subject

For each subject, the study will last a maximum of 34 weeks. This includes the following study period durations:
* Screening Period: *2 weeks up to a maximum of 4 weeks, from the time of informed consent up to randomization and administration of IMP at Baseline (Visit 2).
* Treatment Period: Up to 12 weeks, from the administration of IMP at Baseline (Visit 2) to the assessment of the primary efficacy variable at Week 12 (Visit 11).
* SFU Period: Up to 20 weeks, from the last dose of IMP at Week 10 (Visit 10) to the SFU Visit at Week 30 (Visit 12).
The end of the study is defined as the date of the last visit of the last subject in the study.

Intervention

Patients will receive one of the following treatments; bimekizumab, adalimumab, or placebo (a dummy injection that does not contain any medicine) via injections under the skin (subcutaneously). The injections will last approximately 20 seconds, and will probably be given into the side of abdomen and the outside of upper thighs.
The treatment group that patients are assigned to will be decided by chance (like flipping a coin). Patients will have 50% chance of receiving bimekizumab, 25% chance of receiving adalimumab and 25% chance of receiving placebo. Patient and the study doctor will not know which treatment patient is receiving during the study.

Every patient will receive the below number of injections at the following visits:
At visit 2: 4 injections
At visit 3, 4, 6, 8 and 10: 2 injections
At visit 5, 7 and 9: 1 injection

Study burden and risks

Blood draws: 7 times
Urine tests: 6 keer
SC injections: 17 injections
Skin biopsies: 2 times
Thorax photo or -scan: 1 time (at screening visit)
ECGs: 6 times
The number of visits to the study doctor: 12 visits
Physical examination: 12 times
Questionnaires: psychological, quality of life, status of HS, level of skin pain.

The patient may experience physical or psychological discomfort from the above tests and procedures and questionnaires.
The patient may experience side effects from the study medication.

Contacts

Public
UCB Pharma

Allée de la Recherche 60
Brussels 1070
BE

Scientific
UCB Pharma

Allée de la Recherche 60
Brussels 1070
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

To be eligible to participate in this study, all of the following criteria must be met:
1. An Institutional Review Board (IRB)/Independent Ethics Committee (IEC) approved written Informed Consent Form (ICF) is signed and dated by the subject or by the legal representative.
2. Subject/legal representative is considered reliable and capable of adhering to the protocol (eg, able to understand and complete diaries), visit schedule, and medication intake according to the judgment of the Investigator.
3. Adult subjects (18 to 70 years of age, inclusive) must have a diagnosis of HS for at least 1 year prior to Baseline.
4. Hidradenitis suppurativa lesions must be present in at least 2 distinct anatomic areas, 1 of which must be at least Hurley Stage II or Hurley Stage III.
5. Subject must have stable HS for at least 2 months prior to Screening and also at the Baseline Visit as assessed by the Investigator through subject interview and review of medical history.
6. Subject must have had an inadequate response to at least a 3-month study of an oral antibiotic for treatment of HS (or exhibited recurrence after discontinuation to, or demonstrated intolerance to, or have a contraindication to oral antibiotics for treatment of their HS) as assessed by the Investigator through subject interview and review of medical history.
7. Subject must have a total abscess and inflammatory nodule count *3 at the Baseline Visit.
8. Subject must be considered, in the opinion of the Investigator, to be a suitable candidate

for treatment with adalimumab per regional labeling.
9. Subject must have a C-reactive protein (CRP) level >3mg/L at the Baseline Visit.
10. Subject has a negative tuberculosis (TB) Screening assessment (including an interferon gamma release assay [IGRA] test using QuantiFERON-TB Gold test, or equivalent) and negative posterior-anterior chest x-ray (CXR) or Computed Axial Tomography (CAT) scan of chest at Screening or within 3 months prior to Screening (nuclear magnetic resonance films are not acceptable).
11. Subject must agree to daily use (and throughout the entirety of the study) of 1 of the following over-the-counter topical antiseptics on their HS lesions: chlorhexidine gluconate, triclosan, benzoyl peroxide, or dilute bleach in bathwater.
12. Subject is assessed to have no other medical condition that would preclude their participation in the study, as determined by the Principal Investigator based upon the results of a medical history, physical examination, laboratory profile, and a 12-lead ECG performed during the Screening Period, and confirmed at Baseline.
13. Female subjects must be postmenopausal (at least 1 year; to be confirmed hormonally as part of the Screening process, if less than 2 years since last menstrual period), permanently sterilized (eg, tubal occlusion, hysterectomy, bilateral salpingectomy) or, if of childbearing potential, must be willing to use a highly effective method of contraception up till 20 weeks after last administration of IMP, and have a negative pregnancy test at Visit 1 (Screening) and immediately prior to first dose. The following methods are considered highly effective when used consistently and correctly.
-combined (estrogen and progestogen) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal).
-progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable).
-intrauterine device (IUD).
-ntrauterine hormone-releasing system (IUS).
-bilateral tubal occlusion.
-vasectomized partner (where postvasectomy testing had demonstrated sperm clearance).
-sexual abstinence if it is in accordance with a subject*s preferred and common lifestyle. Subjects who use abstinence as a form of birth control must agree to abstain from heterosexual intercourse until 20 weeks after the last dose of IMP. Study personnel must confirm the continued use of abstinence is still in accordance with the subject*s lifestyle at regular intervals during the study.;Male subjects with a partner of childbearing potential must be willing to use a condom when sexually active, up till 20 weeks after the last administration of IMP (anticipated 5 half-lives).

Exclusion criteria

Subjects are not permitted to enroll in the study if any of the following criteria is met:
1. Prior treatment with anti IL17s or participation in an anti-IL17 study.
2. Subjects who previously received anti-TNFs.
3. Subjects participating in another study of a medication or a medical device under investigation within the last 3 months or at least 5 half-lives of the investigational product, whichever is greater, or is currently participating in another study of a medication or medical

device under investigation.
4. Subject has a known hypersensitivity to any excipient(s) of bimekizumab or adalimumab.
5. Subject is using concomitant oral analgesics for HS-related or non-HS-related pain at study entry:
-Opioid analgesics within 14 days prior to the Baseline Visit.
-Non-opioid oral analgesics unless at a stable dose for at least 14 days prior to the Baseline Visit (PRN use is not considered a stable dose).
6. Subject requires, or is expected to require, opioid analgesics for any reason (excluding tramadol).
7. Subject received prescription topical therapies for the treatment of HS within 14 days prior to the Baseline Visit.
8. Subject received systemic non-biologic therapies for HS with potential therapeutic impact for HS less than 28 days prior to Baseline Visit.
9. Subject has a draining fistula count >20 at the Baseline Visit.
10. Subjects with a diagnosis of inflammatory conditions other than HS, including but not limited to PSO, PsA, RA, sarcoidosis, or systemic lupus erythematosus. Subjects with a diagnosis of CD or ulcerative colitis are allowed as long as they have no active symptomatic disease at Screening or Baseline.
11. Subjects with a history of chronic or recurrent infections, or a serious or life-threatening infection within the 6 months prior to the Baseline Visit (including herpes zoster). Subjects with a high risk of infection in the Investigator*s opinion (eg, subjects with leg ulcers, indwelling urinary catheter, persistent or recurrent chest infections, prior prosthetic joint infection at any time, subjects who are permanently bedridden or wheelchair assisted).
12. Subject has any current sign or symptom that may indicate an active infection (except for common cold), or has had an infection requiring systemic antibiotics within 2 weeks of the Baseline Visit.
13. Any other active skin disease or condition (eg, bacterial, fungal or viral infection) that may interfere with assessment of HS.
14. Subject has history of or current clinically active infection with Histoplasma, Coccidiodes, Paracoccidioides, Pneumocystis, nontuberculous mycobacteria (NTMB), Blastomyces, or Aspergillus or current active Candidiasis (local or systemic).
15. Subject has acute or chronic viral hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV) infection. Subjects who have evidence of, or tested positive for, hepatitis B or hepatitis C are excluded.
-A positive test for the HBV is defined as: 1) positive for hepatitis B surface antigen; or, 2) positive for anti-hepatitis B core antibody.
-A positive test for the 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).
16. Subjects with known TB infection, at high risk of acquiring TB infection, with latent TB infection (LTB), or current or history of NTMB infection (refer to Section 11.3.1 for details on determining full TB exclusion criteria).
17. Subject has a primary immunosuppressive condition, including taking immunosuppressive therapy following an organ transplant, or has had a splenectomy.
18. Subjects with concurrent malignancy or history of malignancy (including surgically resected uterine/cervical carcinoma-in-situ) during the past 5 years will be excluded, with the following exceptions that may be included:
a. *3 excised or ablated, basal cell carcinomas of the skin.

b. One squamous cell carcinoma of the skin (stage T1 maximum) successfully excised, or ablated only (other treatments, ie, chemotherapy, do not apply), with no signs of recurrence or metastases for more than 2 years prior to Screening.
c. Actinic keratosis(-es).
d. Squamous cell carcinoma-in-situ of the skin successfully excised, or ablated, more than 6 months prior to Screening).
19. Subject has a history of a lymphoproliferative disorder including lymphoma or current signs and symptoms suggestive of lymphoproliferative disease.
20. Subject has history of demyelinating disease (including myelitis) or neurologic symptoms suggestive of demyelinating disease.
21. Subjects with a current or recent history, as determined by the Investigator, of severe, progressive, and/or uncontrolled renal, hepatic, hematological, endocrine, pulmonary, cardiac (eg, congestive heart failure, New York Heart Association Grade 3 and 4), gastrointestinal (note: subjects with active peptic ulcer disease are excluded; subjects with a history of peptic ulcer disease are allowed), neurological disease, or inflammatory bowel disease.
22. Subject has a history of uncompensated heart failure, fluid overload, or myocardial infarction, or evidence of new onset ischemic heart disease or (in the opinion of the Investigator) other serious cardiac disease, within 12 weeks prior to the Baseline Visit.
23. Presence of active suicidal ideation, or positive suicide behavior using the *Baseline* version of the Columbia-Suicide Severity Rating Scale (C-SSRS) and the HADS with either of the following criteria:
-Subject has a lifetime history of suicide attempt (including an actual attempt, interrupted attempt, or aborted attempt), or has suicidal ideation in the past 6 months as indicated by a positive response (*Yes*) to either question 4 or question 5 of the *Screening/Baseline* version of the C-SSRS at Screening.
-HADS-D score *10 and HADS-A score *15.
24. Subject has >2x upper limit of normal (ULN) of any of the following: alanine aminotransferase (ALT), aspartate aminotransferase (AST), *alkaline phosphatase (ALP), or >ULN total bilirubin (*1.5xULN total bilirubin if known Gilbert*s syndrome). If subject has elevations only in total bilirubin that are >ULN and <1.5xULN, fractionate bilirubin to identify possible undiagnosed Gilbert*s syndrome (ie, direct bilirubin <35%).
*An isolated elevation between 2xULN and <3xULN of ALP is acceptable in the absence of an identified exclusionary medical condition.
Tests that result in ALT, AST, or ALP up to 25% above the exclusion limit may be repeated once for confirmation during the Screening Period. Upon retesting, subjects whose ALT, AST, or ALP remain above the thresholds defined above, should not be randomized.
For randomized subjects with a Baseline result >ULN for ALT, AST, ALP, or total bilirubin, a Baseline diagnosis and/or the cause of any clinically meaningful elevation must be understood and recorded in the electronic Case Report form (eCRF).
If subject has >ULN ALT, AST, or ALP that does not meet the exclusion limit at Screening, repeat the tests, if possible, prior to dosing to ensure there is no further ongoing clinically relevant increase. In case of a clinically relevant increase, inclusion of the subject must be discussed with the Medical Monitor and/or UCB Study Physician.
25. Subjects with clinically significant laboratory abnormalities (eg, creatinine >1.5xULN, neutropenia <1.5x109/L, hemoglobin <8.5g/dL, lymphocytes <1.0x109/L, platelets <100x109/L). 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 if they are within 25% of the exclusion limit. Upon retesting, subjects whose results remain outside this threshold should not be randomized.
26. Subject has 12-lead ECG with changes considered to be clinically significant upon medical review (eg, QTc using Fridericia*s correction [QTcF] >450ms, bundle branch block, evidence of myocardial ischemia).
27. Subject has received any live (includes 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 or for 20 weeks after the last dose of IMP.
28. Subject has received Bacillus Calmette-Guerin vaccination within 1 year prior to IMP administration.
29. Subject has a history of chronic alcohol or drug abuse within the previous 6 months.
30. Subjects with any other condition which, in the Investigator's judgement, would make the subject unsuitable for inclusion in the study.
31. Subject has previous exposure to adalimumab.
32. Subjects are Investigator site personnel directly affiliated with this study and/or their immediate families. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
33. Subjects are UCB employees or are employees of third-party organizations involved in the study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	16
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Bimekizumab
Generic name:	Bimekizumab
Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	31-10-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Not approved Date:	06-02-2018
Application type:	First submission
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	EUCTR2017-000892-10-NL
ClinicalTrials.gov	NCT03248531
CCMO	NL62797.078.17