A Study to Evaluate the Efficacy and Safety of Bimekizumab in Subjects With Active Ankylosing Spondylitis

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03928743	ACTIVE, NOT RECRUITING	APRIL 26, 2019	MAY 21, 2021

STUDY DESCRIPTION

Brief Summary

The purpose of the study is to demonstrate the efficacy, safety and tolerability of bimekizumab administered subcutaneously (sc) compared to placebo in the treatment of subjects with active ankylosing spondylitis (AS).

Condition or Disease: Ankylosing Spondylitis

Intervention/treatment: Drug: Bimekizumab
Other: Placebo

Phase: Phase 3

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 332 participants

Intervention Model : Parallel Assignment

Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Primary Purpose: Treatment

Official Title: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Bimekizumab in Subjects With Active Ankylosing Spondylitis

Actual Study Start Date: April 2019

Estimated Primary Completion Date: August 2021

Estimated Study Completion Date: August 2022

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Bimekizumab Subjects randomized to this arm will receive bimekizumab during the Double-Blind Treatment Period and the Maintenance Period.	Drug: Bimekizumab Subjects will receive bimekizumab at pre-specified time-points.
Placebo Comparator: Placebo Subjects randomized to this arm will receive placebo during the Double-Blind Treatment Period and receive bimekizumab during the Maintenance Period.	Drug: Bimekizumab Subjects will receive bimekizumab at pre-specified time-points. Other: Placebo Subjects will receive placebo at pre-specified time-points during the Double-Blind Treatment Period.

OUTCOME MEASURES

Primary Outcome Measures: 1. Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response at Week 16 [Time Frame: Week 16]
ASAS40 will be calculated relative to Baseline. The Assessment of SpondyloArthritis International Society (ASAS) criteria for 40% improvement are defined as relative improvements of at least 40%, and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 domains and no worsening at all in the remaining domain. The domains are: Patient's Global Assessment of Disease Activity (PGADA) Pain assessment (the total spinal pain, NRS score) Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI)) Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI))

Secondary Outcome Measures: 1. Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response in TNFα inhibitor-naïve subjects at Week 16 [Time Frame: Week 16]
ASAS40 will be calculated relative to Baseline. The Assessment of SpondyloArthritis International Society (ASAS) criteria for 40% improvement are defined as relative improvements of at least 40%, and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 domains and no worsening at all in the remaining domain. The domains are: Patient's Global Assessment of Disease Activity (PGADA) Pain assessment (the total spinal pain, NRS score) Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI)) Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI))

2. Assessment of SpondyloArthritis International Society 20% response criteria (ASAS20) response at Week 16 [Time Frame: Week 16]
ASAS20 will be calculated relative to Baseline. The Assessment of SpondyloArthritis International Society (ASAS) criteria for 20% improvement are defined as relative improvements of at least 20%, and absolute improvement of at least 1 unit on a 0 to 10 Numeric Rating Scale (NRS) in at least 3 of the 4 following domains and absence of deterioration in the potential remaining domain. The domains are: Patient's Global Assessment of Disease Activity (PGADA) Pain assessment (the total spinal pain, NRS score) Function (represented by Bath Ankylosing Spondylitis Functional Index (BASFI)) Inflammation (the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI))
3. Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) total score at Week 16 [Time Frame: Baseline, Week 16]
The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a validated self-reported instrument, which consists of six 10 unit horizontal Numeric Rating Scales (NRS) to measure the disease activity of ankylosing spondylitis (AS) from the subject's perspective. It measures the severity of fatigue, spinal and peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration) over the last week. The final BASDAI scores ranges from 0 to 10, with lower scores indicating lower disease activity.
4. Assessment of SpondyloArthritis International Society (ASAS) partial remission (PR) at Week 16 [Time Frame: Week 16]
The Assessment of SpondyloArthritis International Society (ASAS) partial remission (PR) is defined as a score of <=2 units on a 0 to 10 unit scale in all 4 domains listed for ASAS20.
5. Ankylosing Spondylitis Disease Activity Score major improvement (ASDAS-MI) at Week 16 [Time Frame: Week 16]
Ankylosing Spondylitis Disease Activity Score major improvement (ASDAS-MI) is achieved when there is a reduction (improvement) >= 2.0 in the Ankylosing Spondylitis Disease Activity Score (ASDAS) relative to Baseline. ASDAS is calculated as the sum of the following components: 0.121 × Total back pain (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Q2 result) 0.058 × Duration of morning stiffness (BASDAI Q6 result) 0.110 × Patient's Global Assessment of Disease Activity (PGADA) 0.073 × Peripheral pain/swelling (BASDAI Q3 result) 0.579 × (natural logarithm of the C-reactive protein (CRP) [mg/L] + 1) Total back pain, PGADA, duration of morning stiffness, peripheral pain/swelling and fatigue are all assessed on a numerical scale (0 to 10 units). High ASDAS scores mean worse disease. If a subjects achieves the ASDAS-MI it indicates a major improvement of their disease.
6. Assessment of SpondyloArthritis International Society (ASAS) 5/6 response at Week 16 [Time Frame: Week 16]
The Assessment of SpondyloArthritis International Society (ASAS) 5/6 response is defined as achieving at least 20% improvement in 5 of 6 domains, including the 4 domains defined for ASAS20 as well as spinal mobility (lateral spinal flexion) and C-reactive Protein (CRP).
7. Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 16 [Time Frame: Baseline, Week 16]
The Bath Ankylosing Spondylitis Functional Index (BASFI) assesses physical function in comprising 10 items relating to activities during the past week. Each item ranges from 0 ('Easy') to 10 ('Impossible'). The BASFI is the mean of the 10 scores such that the total score ranges from 0 to 10, with lower scores indicating better physical function. A negative value in BASFI change from Baseline indicates an improvement from Baseline. The higher the negative value the better the improvement.
8. Change from Baseline in nocturnal spinal pain score Numeric Rating Scale (NRS) at Week 16 [Time Frame: Baseline, Week 16]
Change from baseline in the nocturnal spinal pain NRS at Week 16. Nocturnal spinal pain experienced by ankylosing spondylitis (AS) subjects is measured by one question: pain in the spine at night due to AS?. When responding, the subject is to consider the average amount of pain in the preceding week. It is assessed on a numerical scale (0 to 10 units). A lower score indicates less pain and an improvement of the outcome.
9. Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) total score at Week 16 [Time Frame: Baseline, Week 16]
The Ankylosing Spondylitis Quality of Life (ASQoL), a validated disease-specific 18-item questionnaire, has been developed specifically for measuring health-related quality of life (HRQoL) in subjects with ankylosing spondylitis (AS) and has shown to be responsive in axial spondyloarthritis (axSpA). The ASQoL score ranges from 0 to 18 with a higher score indicating worse HRQoL.
10. Change from Baseline in the Short Form 36-Item Health Survey (SF-36) physical component summary (PCS) score at Week 16 [Time Frame: Baseline, Week 16]
There are 8 SF-36 domain scores. In addition to domain scores, the PCS scores are calculated from the 8 domains. Each of the 8 domain scores and the component summary scores ranging from 0 to 100, with higher scores indicating better health status. A larger positive value in change from Baseline indicates an improvement.
11. Change from Baseline in Bath Ankylosing Spondylitis Disease Metrology Index (BASMI) at Week 16 [Time Frame: Baseline, Week 16]
The Bath Ankylosing Spondylitis Disease Metrology Index (BASMI) characterizes the spinal mobility of subjects with axial Spondyloarthritis (SpA) and Ankylosing Spondylitis (AS). It is a disease-specific measure consisting of 5 clinical measures to reflect subject axial status: cervical rotation; tragus to wall distance; lateral lumbar flexion; lumbar flexion (modified Schober test); intermalleolar distance. According to the linear definition of the BASMI a score of 0 to 10 is calculated for each item based on the measurement. The mean of the sum of the 5 scores provides the BASMI score. The higher the BASMI score the more severe the patient's limitation of movement due to their axial SpA. A negative value in BASMI change from Baseline indicates an improvement from Baseline. The higher the negative value the better the improvement.
12. Change from Baseline in the Maastricht Ankylosing Spondylitis Enthesitis (MASES) Index in the subgroup of subjects with enthesitis at Baseline at Week 16 [Time Frame: Baseline, Week 16]
The Maastricht Ankylosing Spondylitis Enthesitis (MASES) is an index that measures the severity (ie, intensity and extent) of enthesitis through the assessment of 13 entheses (bilateral costochondral 1, costochondral 7, anterior superior iliac spine, posterior iliac spine, iliac crest and proximal insertion of the Achilles tendon sites, and the fifth lumbar vertebral body spinous process) each scored as 0 or 1 and then summed for a possible score of 0 to 13. A higher score indicates worsening.
13. Enthesitis-free state based on the Maastricht Ankylosing Spondylitis Enthesitis Index (MASES) Index in the subgroup of subjects with enthesitis at Baseline at Week 16 [Time Frame: Baseline, Week 16]
The Maastricht Ankylosing Spondylitis Enthesitis (MASES) is an index that measures the severity (ie, intensity and extent) of enthesitis through the assessment of 13 entheses (bilateral costochondral 1, costochondral 7, anterior superior iliac spine, posterior iliac spine, iliac crest and proximal insertion of the Achilles tendon sites, and the fifth lumbar vertebral body spinous process) each scored as 0 or 1 and then summed for a possible score of 0 to 13. A higher score indicates worsening.
14. Incidence of treatment-emergent adverse events (TEAEs) during the study [Time Frame: From Baseline (Day 1) until Safety-Follow-Up (up to Week 72)]
An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.
15. Incidence of treatment-emergent serious adverse events (SAEs) during the study [Time Frame: From Baseline (Day 1) until Safety-Follow-Up (up to Week 72)]
A serious adverse event (SAE) is any untoward medical occurrence that at any dose: Results in death Is life-threatening Requires in patient hospitalisation or prolongation of existing hospitalisation Is a congenital anomaly or birth defect Is an infection that requires treatment with parenteral antibiotics Other important medical events which based on medical or scientific judgement may jeopardise the patients, or may require medical or surgical intervention to prevent any of the above
16. Treatment-emergent adverse events (AEs) leading to withdrawal from investigational medicinal product (IMP) during the study [Time Frame: From Baseline (Day 1) until Safety-Follow-Up (up to Week 72)]
An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
- Male or female patients at least 18 years of age
- Subject has ankylosing spondylitis (AS) as per the Modified New York (mNY) criteria with documented radiologic evidence, and at least 3 months of symptoms with age at symptom onset less than 45 years
- Subjects has moderate-to-severe active disease defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) >=4 AND spinal pain >=4 on a 0 to 10 Numeric Rating Scale
- Subjects had to have either failed to respond to 2 different nonsteroidal anti-inflammatory drugs (NSAIDs) given at the maximum tolerated dose for a total of 4 weeks or have a history of intolerance to or a contraindication to NSAID therapy
- Patients who have taken a tumor necrosis factor alpha (TNFα) inhibitor must have experienced an inadequate response or intolerance to treatment given at an approved dose for at least 12 weeks
- Patients currently taking NSAIDs, cyclooxygenase 2 (COX-2) inhibitors, analgesics, corticosteroids, methotrexate (MTX), leflunomide (LEF), sulfasalazine (SSZ), hydroxychloroquine (HCQ) AND/OR apremilast can be allowed if they fulfill specific requirements prior to study entry

Exclusion Criteria:
- Total ankylosis of the spine
- Treatment with more than 1 TNFα inhibitor and/or more than 2 additional non-TNFα biological response modifiers, or any interleukin (IL)-17 biological response modifier at any time are excluded
- Active infection or history of recent serious infections
- Viral hepatitis B or C or human immunodeficiency virus (HIV) infection
- Any live (includes attenuated) vaccination within the 8 weeks prior to entering the study or TB (Bacillus Calmette-Guerin) vaccination within 1 year prior entering the study
- Known tuberculosis (TB) infection, at high risk of acquiring TB infection, or current or history of nontuberculous mycobacterium (NTMB) infection
- 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
- Diagnosis of inflammatory conditions other than AxSpA, eg, rheumatoid arthritis. Patients with a diagnosis of Crohn's disease, ulcerative colitis, or other inflammatory bowel disease (IBD) are allowed as long as they have no active symptomatic disease when entering the study.
- Presence of active suicidal ideation, or moderately severe major depression or severe major depression
- Female patients who are breastfeeding, pregnant, or planning to become pregnant during the study
- Subject has a history of chronic alcohol or drug abuse within 6 months prior to Screening

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CONTACTS AND LOCATIONS

Contacts

Locations

United States, Arizona	As0011 50052	Phoenix
United States, Arizona	As0011 50058	Phoenix
United States, Arizona	As0011 50062	Sun City
United States, Arizona	As0011 50131	Sun City
United States, California	As0011 50060	Upland
United States, Florida	As0011 50056	Sarasota
United States, Maryland	As0011 50015	Hagerstown
United States, Missouri	As0011 50016	Saint Louis
United States, Oklahoma	As0011 50054	Oklahoma City
United States, Pennsylvania	As0011 50020	Duncansville
United States, Tennessee	As0011 50001	Jackson
United States, Tennessee	As0011 50012	Memphis
United States, Texas	As0011 50057	Dallas
United States, Texas	As0011 50036	Mesquite
Belgium	As0011 40004	Brussels
Belgium	As0011 40003	Genk
Belgium	As0011 40001	Gent
Bulgaria	As0011 40006	Plovdiv
Bulgaria	As0011 40007	Plovdiv
Bulgaria	As0011 40005	Sofia
Bulgaria	As0011 40008	Sofia

China	As0011 20040	Beijing
China	As0011 20021	Chengdu
China	As0011 20019	Guangzhou
China	As0011 20034	Hefei
China	As0011 20024	Nanjing
China	As0011 20018	Shanghai
China	As0011 20020	Shanghai
China	As0011 20026	Shanghai
China	As0011 20025	Wenzhou
Czechia	As0011 40011	Brno
Czechia	As0011 40009	Pardubice
Czechia	As0011 40013	Praha 11
Czechia	As0011 40016	Praha 2
Czechia	As0011 40015	Praha 3
Czechia	As0011 40014	Praha 4
Czechia	As0011 40010	Uherské Hradiště
Czechia	As0011 40012	Zlín
France	As0011 40018	Boulogne-Billancourt
France	As0011 40022	Limoges
Germany	As0011 40025	Berlin
Germany	As0011 40028	Berlin
Germany	As0011 40029	Hamburg
Germany	As0011 40024	Hannover
Germany	As0011 40027	Herne
Germany	As0011 40078	Leipzig
Germany	As0011 40026	Ratingen
Hungary	As0011 40032	Debrecen
Hungary	As0011 40031	Szeged
Hungary	As0011 40080	Szombathely
Hungary	As0011 40033	Székesfehérvár
Japan	As0011 20047	Himeji
Japan	As0011 20065	Kitakyushu
Japan	As0011 20045	Kita
Japan	As0011 20037	Osaka
Japan	As0011 20084	Saga
Japan	As0011 20048	Saitama
Japan	As0011 20031	Sapporo-City
Japan	As0011 20042	Sasebo
Japan	As0011 20032	Suita
Japan	As0011 20030	Tokyo
Japan	As0011 20035	Tokyo
Netherlands	As0011 40034	Amsterdam
Poland	As0011 40038	Elbląg
Poland	As0011 40042	Kraków
Poland	As0011 40037	Lublin

Poland	As0011 40044	Poznań
Poland	As0011 40040	Toruń
Poland	As0011 40041	Warsaw
Poland	As0011 40039	Wrocław
Poland	As0011 40043	Wrocław
Spain	As0011 40045	Coruña
Spain	As0011 40046	Córdoba
Spain	As0011 40047	Madrid
Spain	As0011 40048	Santiago De Compostela
Spain	As0011 40049	Sevilla
Turkey	As0011 40052	Ankara
Turkey	As0011 40053	Ankara
Turkey	As0011 40050	Istanbul
United Kingdom	As0011 40057	Edinburgh
United Kingdom	As0011 40056	Leeds
United Kingdom	As0011 40054	London
United Kingdom	As0011 40055	Norwich

Sponsors and Collaborators

UCB Biopharma SRL

Investigator

Study Director :	UCB Cares	001 844 599 2273 (UCB)

MORE INFORMATION

Responsible Party :	UCB Biopharma SRL
ClinicalTrials.gov Identifier :	NCT03928743
Other Study ID Numbers :	AS0011, 2017-003065-95
First Posted :	April 26, 2019
Last Update Posted :	May 21, 2021
Last Verified :	May 2021
Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	Yes
Plan Description:	Data from this trial may be requested by qualified researchers six months after product approval in the US and/or Europe, or global development is discontinued, and 18 months after trial completion. Investigators may request access to anonymized individual patient-level data and redacted trial documents which may include: analysis-ready datasets, study protocol, annotated case report form, statistical analysis plan, dataset specifications, and clinical study report. Prior to use of the data, proposals need to be approved by an independent review panel at www.Vivli.org and a signed data sharing agreement will need to be executed. All documents are available in English only, for a prespecified time, typically 12 months, on a password protected portal. This plan may change if the risk of re-identifying trial participants is determined to be too high after the trial is completed; in this case and to protect participants, individual patient-level data would not be made available.
Supporting Materials:	Study Protocol, Statistical Analysis Plan (SAP), Clinical Study Report (CSR)
Time Frame:	Data from this trial may be requested by qualified researchers six months after product approval in the US and/or Europe or global development is discontinued, and 18 months after trial completion.
Access Criteria:	Qualified researchers may request access to anonymized IPD and redacted study documents which may include: raw datasets, analysis-ready datasets, study protocol, blank case report form, annotated case report form, statistical analysis plan, dataset specifications, and clinical study report. Prior to use of the data, proposals need to be approved by an independent review panel at www.Vivli.org and a signed data sharing agreement will need to be executed. All documents are available in English only, for a pre-specified time, typically 12 months, on a password protected portal.
URL:	http://www.Vivli.org
Studies a U.S. FDA-regulated Drug Product:	Yes

Studies a U.S. FDA-regulated Device Product:	No	
Product Manufactured in and Exported from the U.S.:	Yes	
Keywords provided by UCB Biopharma SRL:	*Ankylosing spondylitis* *AS Bimekizumab* *Axial spondyloarthritis*	
Additional relevant MeSH terms :	*Spondylitis*	*Spondylitis, Ankylosing*