A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY EVALUATING THE EFFICACY AND SAFETY OF BIMEKIZUMAB IN SUBJECTS WITH ACTIVE ANKYLOSING SPONDYLITIS

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Objective(s): Primary objective:The primary objective is to demonstrate the efficacy of bimekizumab administered subcutaneously (sc) every 4 weeks (Q4W) compared to placebo in the treatment of subjects with active ankylosing spondylitis (AS)....

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

Summary

ID

NL-OMON55807

Source
ToetsingOnline

Brief title
AS0011 235074

Condition

- Autoimmune disorders

Synonym
Active ankylosing spondylitis - Bechterew's disease

Research involving
Human

Sponsors and support

Primary sponsor: UCB Biopharma SRL
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Active ankylosing spondylitis, bimekizumab, Phase 3, subcutaneous

Outcome measures

Primary outcome

Study variables:

Efficacy:

Primary efficacy variable:

SpondyloArthritis International Society 40% (ASAS40) response at Week 16.

Safety:

Primary safety variable:

Not applicable

Secondary outcome

Study variables:

Efficacy:

Secondary efficacy variables:

* ASAS40 response at Week 16 in TNF* inhibitor-naïve subjects

* SpondyloArthritis International Society 20% (ASAS20) response at Week 16

* Change from Baseline in BASDAI total score at Week 16

* ASAS partial remission (ASAS-PR) at Week 16

* Ankylosing Spondylitis Disease Activity Score major improvement (ASDAS-MI) at Week 16

* Assessment of SpondyloArthritis International Society 5 out of 6 response criteria (ASAS5/6) response at Week 16

* Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 16

* Change from Baseline in nocturnal spinal pain score (NRS) at Week 16

* Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) total score at Week 16

* Change from Baseline in the Short Form 36-Item Health Survey (SF-36) physical component summary (PCS) score at Week 16

* Change from Baseline in Bath Ankylosing Spondylitis Disease Metrology Index (BASMI) at Week 16

* Change from Baseline in the Maastricht Ankylosing Spondylitis Enthesitis (MASES) Index in the subgroup of subjects with enthesitis at Baseline at Week 16

* Enthesitis-free state based on the MASES Index in the subgroup of subjects with enthesitis at Baseline at Week 16

Other (exploratory) efficacy variables:

* ASAS40 response

* Time to ASAS40 response

* ASAS20 response

* Time to ASAS20 response

* ASAS5/6 response

* ASAS-PR

* Change from Baseline in Ankylosing Spondylitis Disease Activity Score

C-reactive protein (ASDAS-CRP)

* ASDAS status (eg, inactive disease, low disease, high disease, and very high

disease)

* ASDAS-MI

* Change from Baseline in BASDAI total score

* BASDAI50 response

* Change from Baseline in BASFI

* Change from Baseline in the MASES Index in the subgroup of subjects with

enthesitis at Baseline

* Enthesitis-free state based on the MASES in the subgroup of subjects with

enthesitis at Baseline

* Change from Baseline in BASMI

* Change from Baseline in Physician*s Global Assessment of Disease Activity

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

* Change from Baseline in total and nocturnal spinal pain score (NRS)

* Change from Baseline in the average score of Questions 5 and 6 of the BASDAI

concerning morning stiffness

* Change from Baseline in CRP

* Responses to the European QoL-5 Dimensions 3-Level (EQ-5D-3L)

* Change from Baseline in EQ-5D-3L visual analog scale scores

* Change from Baseline in the EQ-5D utility score

* Change from Baseline in the SF-36 PCS score

* Change from Baseline in the SF-36 mental component summary (MCS) score

* Change from Baseline in sleep quality score (Medical Outcomes Study [MOS

12-item] scale)

* Change from Baseline in Functional Assessment of Chronic Illness Therapy

(FACIT)-Fatigue subscale score

* Change from Baseline in ASQoL total score

* Change from Baseline in the Work Productivity and Activity Impairment

Questionnaire specific health problem

* Change from Baseline in PHQ-9

* Change from Baseline in (44/44) tender joint count and swollen joint count

* Change from Baseline in Ankylosing Spondylitis spine MRI-activity

(ASspiMRI-a) in the Berlin modification score

* Change from Baseline in sacroiliac joint Spondyloarthritis Research

Consortium of Canada score

Safety:

Secondary safety variables:

* Incidence of treatment-emergent adverse events (TEAEs)

* Incidence of treatment-emergent serious adverse events (SAEs)

* TEAEs leading to withdrawal from IMP

Other (exploratory) safety variables:

* Change from Baseline in vital signs (blood pressure, temperature, and pulse rate)

* Standard 12-lead electrocardiogram results

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

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

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

Other exploratory variables:

Pharmacokinetic exploratory variable:

The plasma concentration of bimekizumab.

Pharmacogenomic exploratory variables:

Genomic, genetic, epigenetic, proteins, and metabolite biomarkers may be measured to evaluate the relationship with response to treatment with bimekizumab, axSpA disease biology, bone metabolism, and inflammatory and immune response processes.

Immunological exploratory variables:

* Anti-bimekizumab antibody status

* Treatment emergent antibody positivity derived from anti-drug antibody assays

Study description

Background summary

axSpA epidemiology
Axial SpA is a chronic inflammatory disease that impacts a substantial proportion of the population. Limited evidence exists regarding the global occurrence of axSpA with a prevalence of 0.20 to 0.25% in Europe and North America, and a wider range in Asia (0.06 to 0.20%) (Stolwijk et al, 2016); however, recent data suggest that the prevalence is similar to that of RA in the US (axSpA: 0.7% to 1.4%; RA: 0.5% to 1.0%) (Reveille et al, 2012; Myasoedova et al, 2010; Helmick et al, 2008). Axial SpA comprises those diseases with mainly axial involvement (sacroiliac joints and spine), including AS and nr-axSpA.

Current treatments for axSpA
Nonsteroidal anti-inflammatory drugs are used as first-line treatment and are effective for the symptoms (pain and stiffness) of axSpA (van der Heijde et al, 2017; Ward et al, 2015; Poddubnyy, 2013; Poddubnyy et al, 2012), but many patients lose or never have clinically meaningful response and structural damage often progresses despite their use. Conventional disease-modifying antirheumatic drugs (DMARDs, eg, methotrexate [MTX] and sulfasalazine [SSZ]) have no proven efficacy in axial disease, but may benefit patients with peripheral joint disease (Haibel et al, 2007; Braun et al, 2006; Haibel et al, 2005). Therefore, DMARDs are recommended only in patients with predominantly peripheral manifestations (Braun et al, 2011).
Patients who are intolerant of or have inadequately responded to NSAIDs, or those in whom NSAIDs are contraindicated, have approved treatment options such as tumor necrosis factor alpha (TNF*) inhibitors (van der Heijde, 2017; Ward et al, 2015). Recently, the interleukin (IL)-17 cytokine family has been identified as a therapeutic target in axSpA and secukinumab, an IL-17A monoclonal antibody, has recently been approved as a treatment option in active AS.

Bimekizumab
Bimekizumab (UCB4940) is an engineered, humanized full-length monoclonal antibody of IgG1 subclass of approximately 150,000 Dalton, which is expressed in a genetically engineered Chinese Hamster Ovarian (CHO) cell line. Bimekizumab has high affinity for human IL-17A and human IL-17F and selectively and potently inhibits the activity of both isoforms in vitro. Interleukin-17A and IL-17F are key proinflammatory cytokines believed to play important roles in autoimmune and inflammatory diseases. Therefore, bimekizumab permits an

evaluation of the potential for additional efficacy, which may be conferred by dual inhibition of both cytokines, in patients suffering from diseases in which both cytokines are active. Bimekizumab is being developed for the treatment of patients with inflammatory diseases such as PsA, psoriasis (PSO), axSpA and hidradenitis suppurativa.

Study objective

Objective(s):

Primary objective:
The primary objective is to demonstrate the efficacy of bimekizumab administered subcutaneously (sc) every 4 weeks (Q4W) compared to placebo in the treatment of subjects with active ankylosing spondylitis (AS).
Secondary objectives:
The secondary objectives of the study are as follows:
* To assess the efficacy of bimekizumab compared to placebo
* To assess the safety and tolerability of bimekizumab
* To assess the impact of bimekizumab on patient-reported quality of life
* To assess the impact of bimekizumab on spinal mobility
* To assess the impact of bimekizumab on enthesitis and on peripheral arthritis

Other objectives:
The other objectives are as follows:
* To assess the immunogenicity of bimekizumab
* To assess the pharmacokinetics (PK) of bimekizumab
* To assess the maintenance of efficacy of bimekizumab
* To assess the relationship between exploratory biomarkers, drug treatment, and AS disease biology
* To assess the impact of bimekizumab on work productivity
* To assess the impact of bimekizumab on inflammatory changes using magnetic resonance imaging (MRI)

Study design

Study design and methodology:

This is a multicenter, Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in eligible subjects with active AS. The study will include 3 periods: a Screening Period (*14 days to *35 days), a Treatment Period (52 weeks) consisting of a 16-week Double-Blind Treatment Period and a 36 week Maintenance Period, and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]) (ie, Week 48 for subjects who completed AS0011; for subjects not entering the extension study or who discontinue early, including those withdrawn from study treatment). The maximum study duration per subject

will be 73 weeks.
During the Double-Blind Treatment Period, subjects will be randomized in a 2:1 fashion (stratified by region and prior TNF* inhibitor experience) to 1 of 2 treatment arms to receive blinded IMP regimens of bimekizumab 160 mg sc Q4W or placebo sc Q4W.
The Double-Blind Treatment Period ends after Week 16 assessments. At Week 16, subjects will transition from the double-blind, placebo-controlled treatment into the 36-week Maintenance Period with bimekizumab treatment. The 36-week Maintenance Period starts with the Week 16 IMP administration. All subjects will receive bimekizumab 160 mg sc Q4W during the Maintenance Period. Starting at Week 20, nonbiologic rescue therapy for axial spondyloarthritis (axSpA) may be adjusted or added, at the Investigator*s discretion, while continuing bimekizumab.

Subjects completing Week 52, who are not withdrawn from IMP, may be eligible for enrollment in an extension study with bimekizumab. Subjects who are ineligible for or choose not to participate in the extension study at Week 52, will undergo a SFU Visit. Subjects withdrawing from the IMP will have an Early Termination Visit and a SFU Visit 20 weeks after the final dose of IMP, as applicable.
Interim analyses of all available data (including efficacy, safety, and pharmacokinetic [PK]) will be conducted after the planned number of randomized subjects have completed 24 weeks and 52 weeks of treatment or have withdrawn from IMP or the study. The final analysis of all available data will be performed after all randomized subjects have completed the SFU Visit or have withdrawn from the IMP and/or study.

Intervention

Treatment(s), dose(s), mode of administration, and duration:
During the Double-Blind Treatment Period, bimekizumab or placebo will be administered to subjects by the unblinded study personnel at the study site as per dosing schedule given below:
* Bimekizumab 160 mg sc at Week 0 (Baseline) followed by bimekizumab 160 mg sc Q4W at Weeks 4, 8, and 12
* Placebo sc at Week 0 (Baseline) followed by placebo sc Q4W at Weeks 4, 8, and 12.

During the Maintenance Period, bimekizumab will be administered to subjects by the blinded or unblinded study personnel at the study site, according to the site-specific blinding plan, as per dosing schedule given below:
* Subjects who received bimekizumab 160 mg sc Q4W during the 16 week Double Blind Treatment Period will continue to receive bimekizumab 160 mg sc Q4W.
* Subjects who received placebo during the 16 week Double Blind Treatment Period will be re allocated to bimekizumab treatment. After the Week 16 assessments are performed, all subjects will receive bimekizumab 160

mg sc at the Week 16 Visit.
Unblinded study personnel will be responsible for recording the administration information on source documents, and administration of the IMP as sc injections. The unblinded personnel will not be involved in any other aspect of the study.

Study burden and risks

WHAT PARTICIPATION INVOLVES
In total your participation in this study will be up to 73 weeks (approximately 1.5 year). You will have to come to the clinic for up to 18 visits (most visits occur every 4 weeks).
The study consists of 3 periods:
* a screening
* a treatment (52 weeks) and maintenance (36 weeks: from Week 20 to Week 52)
* a final Safety Follow-Up Visit (this will be done 20 weeks after the final dose of the study drug). A final Safety Follow-Up visit is required:
* if you complete the study up to Week 52 and do not enter the extension study. More information about this extension study is explained under the header *treatment*.
* if you are withdrawn from the study drug and return for all scheduled visits up to Week 52.
* if you withdraw consent and do not return for all scheduled visits you will still be encouraged to return for a final safety assessment.

Screening
Your first visit will be the screening visit. At this visit your study doctor will explain the study and answer any questions you may have. After reading this Patient Information Form and if you agree to participate in this study, you will be asked to sign the Informed Consent Form at the end of this document. You must give your written informed consent before you undergo any study-related activities including screening procedures. During this visit, some tests will be conducted.
The Screening Period will last for at least 2 weeks and up to 5 weeks to perform all required assessments to determine if you can participate in the study. This period can be repeated if some of your test results need to be repeated, or you may be asked to stop the intake of certain drugs that are not allowed to be taken while taking part in the study.
The following procedures will be done during the screening visit:
* The study doctor will check that you are eligible to take part in the study.
* Your study doctor will ask your personal information such as your age, sex ,complete history of lifestyle (alcohol, smoking, and drug consumption).
* Your study doctor will also ask your AS history, any other medical history, what medicines you take now and had taken before, and your current medical conditions.
* You will be asked about any health problems or other medical conditions that you may have had.

* You will be asked to fill in several questionnaires at the visits. You will be given an electronic device (tablet) to record your answers to the questionnaires during the visits. These questionnaires will be repeated throughout the course of the study to monitor if the study drug has any impact on your mental health.
* You will be asked questions about symptoms of Tuberculosis and potential exposure to Tuberculosis. Tuberculosis is also called TB and it is an infectious disease (caused by a bacterium) mainly of the lung, but it can affect other areas of the body. TB bacteria may be present in your body but not yet causing an infectious disease, this is referred to as "latent" TB. If latent TB is diagnosed, you can participate in this study only after receiving appropriate treatment for TB infection. A chest X-ray will be taken (unless you have had a chest X-ray in the previous 3 months and the report is available). The chest X-ray must be clear of signs of TB infection (previous or current) before first study drug administration.
* Your vital signs (blood pressure, pulse rate, and body temperature) will be measured.
* Your weight and height will be measured. During this measurement, you will be asked to remove your footwear.
* An electrocardiogram (ECG - is a painless, non-invasive test that shows how your heart works, it takes a picture of the electrical activity of your heart) will be performed.
* A blood sample will be obtained for routine laboratory examinations to learn about your general health and body functions, and for pregnancy test in women who are able to have children.
* A blood sample will be obtained to test for hepatitis B and C, the human immunodeficiency virus (HIV), TB, and HLA-B27 (human leukocyte antigen B27, a protein in the blood). Hepatitis B and C are viruses that can damage the liver. HIV is the virus that can cause the acquired immune deficiency syndrome (AIDS). Positive results for hepatitis or HIV will be reported to health authorities as per the local requirements. In case you have a positive result, you are encouraged to discuss with your study doctor what further medical care may be applicable to you. If you have any questions about these tests, please ask the study doctor or study staff.
* A urine sample will be obtained for routine laboratory examinations and screening for drugs.
* An X-ray of the joint will be taken to confirm your eligibility for the study (unless you have had a joint X-ray performed any time prior to Screening).
* X-ray of your spine will be taken (unless you have had spine X-ray within 6 months prior to Screening) to assess your disease progression.
* An MRI scan of the joint and spine will be performed at this visit if you agreed to participate in the MRI sub-study by signing the MRI sub-study consent form.
* An additional blood samples and/or stool sample will be collected if you agreed to participate in the genetic/biomarker sub-study by signing the genetic/biomarker sub-study consent form.

* Additionally, you will also be asked if you would like to participate in an optional genetic/biomarker sub-study and/or an MRI sub-study that are being run within the main study. Additional blood samples and/or stool samples will have to be taken for the genetic/biomarker sub-study. For the MRI sub-study, you have to undergo additional MRI scans. If you wish to take part in the sub studies, you will be given an extra sub-study Patient Information Sheet and Informed Consent Form to read and sign. The study doctor will discuss this with you and will answer any questions you might have. Your refusal to participate in any sub-study will not affect your ability to participate in the main study. However, the knowledge gained from this research may help in the development of new therapies for all patients with AS.

Treatment
After all the Screening procedures have been done, and it is found that you can take part in the study, you will be entering the Treatment Period and receive your first dose of study drug at the end of the Baseline Visit.
Duration of the Treatment Period is 52 weeks and includes 2 stages:
* Double-Blind Treatment Period of 16 weeks, and
* Maintenance Period of 36 weeks
During the Double-Blind Treatment Period, you will be randomly assigned like drawing straws from a hat to receive either bimekizumab, or a placebo for 16 weeks. You will receive either of them in a double blind fashion. *Double-blind* means that neither you nor the staff at the clinical site will know which treatment you are receiving. You will have a 66% chance of receiving bimekizumab and 33% chance of receiving placebo.
The assigned study drug will be given to you as an injection under the skin. Each injection will last approximately 10 to 15 seconds and will be given on either your tummy, upper arm or the outside of your upper thighs. The injection site will be rotated between visits. Injections will not be in the areas where skin is tender, red, bruised, and hard.
There are 4 injection days during the treatment period: Baseline (Day 1), Week 4, Week 8, , and Week 12. In case you are not able to visit the clinic on your scheduled day, you can visit the clinic either 3 days before or 3 days later than the scheduled visits date after discussing with your study doctor. During these visits, the questionnaires will be completed at first and the injection will be given after completion of all study assessments on the specified days.

During the Maintenance Period all study patients will receive bimekizumab
The assigned study drug will be given to you as an injection under the skin every 4 weeks over a period of 36 weeks.
There are 9 injection days during the maintenance period. In case you are not able to visit the clinic on your schedule day, you can visit the clinic either 4 days before or 4 days later the scheduled visits date after discussing with your study doctor.
If you qualify and if you agree, you may be invited to participate in an extension study if you have been treated with study drug up to Week 52. The

study doctor will let you know if you qualify for the extension study.
At the completion of the maintenance period, the study doctor will discuss with you the treatment options for you. There will be an extension study for patients who complete this study, in which patients can receive the study treatment. If you complete this study and are considered eligible by the study doctor, you will be able to take part in the extension study with written informed consent. Study drug will be administered for the patients who agree to take part in the extension study at Week 52 Visit.

Early Termination Visit:
An Early Termination Visit will be performed if you are leaving the study much earlier than the study completion, either because you decided to discontinue by yourself, or because of safety issues regarding your personal health as determined by your study doctor.
Safety Follow-Up Visit (if applicable):
This final visit will take place 20 weeks after your last injection of study drug. In case you are not able to visit the clinic on your scheduled day, you can have the visit either within 3 days before or 7 days later the scheduled visit date after discussing with your study doctor.
* You will have this visit if you have withdrawn from the study early or if you have completed the study and are not taking part in the extension study. If you take part in the extension study, you will not have this visit. This visit marks the end of your study participation and serves to check on your health status.

Unscheduled Visit:
If the study doctor considers that an Unscheduled Visit is needed for your safety and wellbeing, you will be requested to complete it at any time during the study but prior to the Safety Follow-Up Visit. Additional assessments may be performed during the Unscheduled Visit(s) at the study doctor's discretion to protect your safety and wellbeing.

Rescue therapy:
You may require add-on therapies referred to as Rescue therapy, this will be determined by your study doctor. You may receive rescue therapy while continuing to receive the study drug dose, anytime from Week 20 onwards. Rescue therapy may include only the following options, no other medication changes or additions are permitted for rescue therapy. The options are,
* Start, stop or alter the anti-inflammatory drugs, anti-rheumatic drugs and/or joint injections that are taken at baseline or any visit.
* A decrease in the dosage of the agent taken for the treatment AS.

More information on all tests and examinations performed during the visits can be found in Appendix C of the main PIF.

POSSIBLE SIDE EFFECTS, RISKS AND DISCOMFORTS
Like all drugs, the study drug being tested may cause side effects. In

addition, the study drug may involve risks that are currently unknown. In the data from the completed studies, most of the side effects were mild to moderate, easily manageable, resolved and did not require discontinuation of the treatment. These side effects included:
* Very Common (occurring in more than 1 in 10 patients):
* Upper respiratory tract infections (such as a common cold and runny nose) which were all mild or moderate.

* Common (occurring between 1 and 10 in 100 patients):
* Less blood cells called neutrophils which help to fight infections
* Headache
* Tiredness
* Fungal infections of the skin or mucous membranes, mostly in the mouth. If you develop symptoms of a fungal infection, particularly in the mouth or throat (creamy white bumps or patches on your tongue, inner cheeks, gums or throat; bad taste in your mouth; pain or difficulty while swallowing), you must tell your study doctor immediately so appropriate action can be discussed
* Fungal infections of the skin or nails (e.g. ringworm, athletes' foot, jock itch, etc.)
* Ear infections
* Herpes simplex infections, a virus that may causes sores on the skin, mouth, lips, eyes and genitals
* Intestinal infections
* Inflamed hair follicles
* Red, itchy, dry, cracked skin

In studies where patients received the study drug for a period of a year or longer, upper respiratory tract infections, runny nose and fungal infections of the mouth were the most frequent side effects.

You may have an allergic reaction to the study drug. Although serious allergic reactions have not yet been seen in the patients receiving this study drug, signs may include a skin rash, swelling of the face, tongue, lips, or throat, or having trouble breathing. If you have any of these signs, you must go to an Emergency department immediately and make sure that your study doctor is informed.

In rare instances, study participants taking the study drug have developed inflammatory bowel disease or have had a worsening (flare) of existing underlying disease. Symptoms such as persistent bloody diarrhea with urgency or crampy abdominal pain may indicate the development or worsening of inflammatory bowel disease. If you develop these symptoms you must tell your study doctor immediately so appropriate action can be discussed.

Less common side effects and the risk and discomforts of the tests and procedures
Uncommon Side effects (occurring in more than 1 in 1000 to less than 1 in 100

patients):
- Injection site reactions (such as redness, pain and swelling)
- Liver problems. If this happens to you during the study, extra testing of blood and urine will be done to try and understand the cause and best treatment for this
- Acne

Risk and discomforts of the tests and procedures:
* Vital signs recording: An inflatable cuff will be placed on your arm and a machine will measure your blood pressure and pulse rate, after you have been sitting down for 5 minutes. You may experience mild discomfort in your arm while the cuff is inflated.
* Blood samples: Throughout the study, approximately 24 mL of blood will be taken per visit. A total of approximately 238 mL (about half of what you give during blood donation) will be taken throughout the study for regular study visits. In case you are participating in genetic/biomarker sub study the total volume would increase to 297 mL (about half of what you give during blood donation). If necessary, additional blood samples may be collected during the study at the study doctor's discretion to protect your safety and wellbeing.
* During the collection of blood samples, you may experience slight discomfort and a small amount of bleeding, discoloration or bruising at the site where the needle was inserted. Clot formation and infections may occur at the puncture site, but this is extremely rare. Fainting may occur during or shortly after having blood drawn. If faintness is experienced, you should lie down immediately to avoid possible injury caused by falling, and notify the site research staff. In very rare cases nerve damages may occur.
* Under the skin injection and injection site reactions: For most people, needle punctures for injections do not cause any serious problems. Sometimes they may cause bleeding or bruising where the injection is given. Sometimes people complain of discomfort and/or pain at the site of the injection. Rarely, injections may cause skin and/or soft tissue infections. Additionally, if a blood vessel is entered by the needle, the risk of infection could include germs entering into the blood system, which can be very serious. The risk of this happening is low.
* Electrocardiogram (ECG): You will be requested to disrobe from the waist up in order to ensure correct ECG recording. You may experience slight skin irritation from the adhesive on the ECG electrodes, but this is generally mild and clears up within a few days.
* Mental health problems and/or depression: Some patients who have psoriasis, psoriatic arthritis, AS and hidradenitis suppurativa suffer from psychological problems like depression. You will be asked to complete questionnaires at all visits about how you are feeling mentally and if you have had any thoughts of hurting yourself at each visit/during the study to monitor your mental health status. Tell the study doctor if you feel important changes in your mood or if you experience psychological problems.
* Vaccines: Please tell your study doctor if you are planning to get

vaccinated, as some types of vaccinations are not allowed prior to dosing, during the study and for up to 20 weeks after the last dose of the study drug.
* Private medical insurance: If you hold private medical insurance, you are advised to check with the company who provides this insurance before agreeing to take part. This is to make sure that your medical insurance will not be affected by being in a clinical study.

Exposure to radiation
X-ray * Chest, sacroiliac joint and spine: You will be exposed to a low level of radiation. The total amount of radiation you will be exposed to in this study is approximately 1.5 mSv. To compare: the background radiation in the Netherlands is ~2.5 mSv per year. If you participate in scientific research involving exposure to radiation more often, you should discuss with the investigator whether participation at this moment would be safe. The radiation used during the study may lead to damage to your health. However, this risk is small. We nevertheless advise you not to participate in another scientific study involving exposure to radiation in the near future. Examinations or procedures involving radiation for medical reasons are not a problem. You must not have an X-ray if you think you could be pregnant. Please inform your study doctor accordingly.
The risk associated with having an MRI of the spine and joints is very minimal. However, if you are claustrophobic (have a fear of closed spaces) or have had any metal placed in your body (for example, during a surgery), you should tell your doctor.

Contacts

Public
UCB Biopharma SRL

Allée de la Recherche 60
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Scientific
UCB Biopharma SRL

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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 patients at least 18 years of age, -Subject has ankylosing spondylitis 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, -Patients had to have either failed to respond to 2 different NSAIDs given at the maxiumum tolereated dose for a total of 4 weeks or have a history of intolerence to or a contraindication to NSAID therapy.-Patients who have taken a tumor necrosis factor alpha (TNF*) 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 TNF* inhibitor and/or more than 2 additional non-TNF* 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 AS, 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

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):	16-01-2020
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bimekizumab
Generic name:	bimekizumab

Ethics review

Approved WMO Date:	13-03-2019
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-07-2019
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-06-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-06-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-06-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-08-2020

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-02-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-04-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-01-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2017-003065-95-NL
ClinicalTrials.gov	NCT03928743
CCMO	NL69337.028.19