A Phase-IV, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Trial to Evaluate the Efficacy and Safety of Golimumab (MK-8259 [SCH 900259]) After Treatment Withdrawal, Compared With Continued Treatment (Either Full- or Reduced-Treatment Regimen), In Subjects With Non-Radiographic Axial Spondyloarthritis

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Primary objectives and hypotises: In adults with active nr-axSpA who attain inactive disease after receiving open-label golimumab during a 10-month run-in (Period 1):Primary Objective: To evaluate the effect of treatment withdrawal vs continued...

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

Summary

ID

NL-OMON47719

Source
ToetsingOnline

Brief title
Golimumab-MK8259-GO-BACK

Condition

- Autoimmune disorders

Synonym
axiale spondyloarthritis., rheumatic disease

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Merck Sharp & Dohme

Intervention

Keyword: Axial spondyloartritis, efficacy and safety, Golimumab

Outcome measures

Primary outcome

The primary efficacy endpoint for this trial is the proportion of subjects without a disease activity *flare* during up to 12 months in Period 2 (in subjects who attained inactive disease status after receiving open-label golimumab in Period 1).

A *flare* is defined as ASDAS at two consecutive visits that both show either absolute score >=2.1 or post-withdrawal increase (i.e., change from Visit 23) of >=1.1.

Secondary outcome

During Period 2:

- Proportion of subjects with a *flare* in the treatment-withdrawal group or the reducedtreatment group who then show a clinical response after re-treatment

with open-label golimumab;

- Time to a first *flare*;

- Proportion of subjects achieving ASAS20 response;

- Proportion of subjects achieving ASAS40 response;

- Proportion of subjects achieving BASDAI50 response;

- Proportion of subjects achieving ASAS partial remission;

- Proportion of subjects achieving inactive disease status: ASDAS <1.3 score.

for exploratory endopints please refer to protocol chapter 8.4.1.3

Study description

Background summary

The current paradigm for treatment of nr-axSpA with TNF inhibitors is to maintain treatment on a chronic basis. Data regarding alternate treatment paradigms with TNF inhibitors for the long-term management of nr-axSpA are not available. An example of an alternate treatment paradigm is to adjust the dosing regimen, guided by clinical symptoms and signs. The purpose of this trial is to evaluate the effects of golimumab treatment withdrawal, compared with continued golimumab treatment (either QM or Q2M), during approximately up to 12 months. Efficacy and safety results of this trial will provide investigators and clinicians with important information regarding dose optimization of golimumab for treatment of nr-axSpA, especially for subjects who show a good response to golimumab within 4 months and then have inactive disease status after both 7 and 10 months of open-label treatment in Period 1.

Study objective

Primary objectives and hypotises:
In adults with active nr-axSpA who attain inactive disease after receiving open-label golimumab during a 10-month run-in (Period 1):

Primary Objective: To evaluate the effect of treatment withdrawal vs continued treatment with golimumab (either QM or Q2M) on the incidence of a *flare*

during up to 12 months of Period 2.

Hypothesis: Continued treatment with golimumab is superior to treatment withdrawal, based on the proportion of subjects without a *flare* during up to 12 months of Period 2.

Secondary Objective(s) & Hypothesis(es)
In subjects who withdraw from or continue treatment with golimumab during Period 2:

(1) Objective: To characterize the proportion of subjects with a *flare* in the treatmentwithdrawal group or the reduced-treatment group who then show a clinical response after retreatment with open-label golimumab.

(2) Objective: To evaluate the time to first *flare* after withdrawal of golimumab vs continuous treatment with golimumab (either QM or Q2M).

(3) Objective: To evaluate the symptoms and signs of nr-axSpA (e.g., Assessment of SpondyloArthritis international Society [ASAS]20, ASAS40, BASDAI50, ASAS partial remission and ASDAS <1.3) after withdrawal of golimumab vs continuous treatment with golimumab (either QM or Q2M) and after re-treatment with openlabel golimumab if needed for a *flare*.

(4) Objective: To characterize the safety and tolerability of golimumab treatment.

Study design

This is a randomized, double-blind, parallel-group, withdrawal trial of golimumab (MK-8259) in subjects with nonradiographic axial spondyloarthritis (nr-axSpA) to be conducted in conformance with Good Clinical Practices (GCPs). In brief, subjects with active nr-axSpA are treated with open-label golimumab. Those subjects who attain inactive disease status when assessed after both 7 and 10 months on open-label therapy are then randomized to be either withdrawn from golimumab or continued on golimumab using either a full (every month [QM]) or a reduced (every 2 months [Q2M]) regimen. Randomized subjects are followed for approximately 12 months to characterize the incidence of a *flare* in disease
activity. Those subjects who have a disease *flare* following randomization are then retreated with open-label golimumab to characterize the clinical response to re-treatment after a *flare*.

For more detailed informatie please refer to chapter 2 of the protocol.

Intervention

First 10 months open label treatment of golimumab, monthly administration of 50 mg.

Then 12 months dubble blind fase:
- Treatment withdrawal: Placebo every month (QM)
- Golimumab every month (QM)
- Golimumab every 2 months (Q2M)

Study burden and risks

Golimumab has been shown to be effective and generally safe and well -tolerated in subjectsfor the treatment of nr-axSpA. THis is used for standard treament for the patients and the risk for side effects is similiar in when participating in the trial. Patient may have to come more often to the hospital becose of assessments and they will be asked to complete questionnaires. Please refer to protocol section 4.3 for details of risks and benefits.

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

1.Be male or female and must be >= 18 to <= 45 years of age;2.Be able to provide written informed consent for the trial and may also provide consent for Future Biomedical Research. However, the subject may participate in the trial without participating in Future Biomedical Research;3. Meet one of the following categories:;a) The subject is not of reproductive potential, defined as a male who has azoospermia OR as a female who is either: (1)Postmenopausal (2) has had a hysterectomy and/or bilateral oophorectomy, bilateral salpingectomy, or bilateral tubal ligation/occlusion; OR (3) has a congenital or acquired condition that prevents childbearing.;b) The subject is a female or a male who is of reproductive potential and agrees to avoid becoming pregnant or impregnating a partner while receiving trial medication or within 6 months after the last dose of trial medication by complying with one of the following: (1) practice abstinence* from heterosexual activity OR (2) use (or have their partner use) acceptable contraception during heterosexual activity.;Acceptable methods of contraception are defined in the protocol.;4.Have chronic back pain of >=3 months duration by history;5.Have a physician*s diagnosis of active nr-axSpA with disease duration <=5 years;6.Meet either criterion *a* or *b* as adopted from ASAS classification criteria: a)Active inflammation on MRI highly suggestive of sacroiliitis associated with spondyloarthropathy and 1 or more of the spondyloarthritis;characteristics as described in the protocol. b)HLA-B27+ gene and 2 or more of the spondyloarthritis characteristics as described in the protocol;7.Have elevated CRP at the Screening visit or evidence of active inflammation in the SI joints on MRI;8.Have ASDAS >=2.1 at the Screening visit;9.Show high disease activity at Screening and Baseline of both a Total Back Pain score of >=4 and a BASDAI score of >=4 (each on a NRS of 0 to 10);10.Have an acceptable history of use of NSAIDs: either an inadequate response, as assessed by the investigator, with maximal recommended daily doses of at least 2 NSAIDs; or must be unable to receive maximal NSAID therapy because of intolerance, toxicity, or contraindications to NSAIDs. (Note: It is possible that a subject had a good response initially to NSAIDs but subsequently had inadequate response or developed intolerance to NSAIDs therapy);11.Have acceptable current use of NSAIDs at Screening: a)If currently using an NSAID, must be on a stable daily dose for at least 14 days prior to Screening b)If not currently using an NSAID, short-term use is allowed (up to 1 week) during Period 1 and is allowed as needed during Period 2;12.Have no history of untreated latent or active tuberculosis;13.Be judged to be medically stable, other than nr-axSpA, based on medical history, physical examination, and routine laboratory tests;14.Undergo screening for hepatitis B virus (HBV), which at a minimum includes testing for HBV surface antigen (HBsAg), HBV surface antibody (anti-HBs), and HBV core antibody (anti-HBc total), and demonstrate to be eligible based on the results as described in the protocol

Exclusion criteria

1.Has bilateral sacroiliitis Grade 2 or unilateral sacroiliitis Grade 3 or Grade 4 on conventional x-rays (to exclude subjects who meet modified New York criteria for AS);2.If female, is nursing, pregnant, or intending to become pregnant within 6 months after receiving the last administration of trial medication;3. Intends to donate eggs (female subjects) or sperm (male subjects) while receiving trial medication or within 6 months after the last dose of trial medication.;4.Has any clinically significant condition or situation, other than those listed as exclusion criteria that, in the opinion of the investigator, would interfere with the trial evaluations or participation in the trial;5.Has ever received any cytotoxic drugs, including but not limited to chlorambucil, cyclophosphamide, nitrogen mustard, or other alkylating agents;6. Has received any treatment as described in the protocol more recently than the indicated offdrug period prior to Screening;7.Has ever received TNF-α targeted therapy or any other biological agents intended to treat immune-mediated diseases, including but not limited to infliximab, etanercept, adalimumab, certolizumab, golimumab, alefacept, efalizumab, rituximab, natalizumab, secukinumab, ixekizumab, ustekinumab, or vedolizumab;8.Has an allergy/sensitivity to golimumab or its excipients;9.Has any systemic inflammatory condition from Screening up to Baseline with signs and symptoms including, but not limited to: a. psoriatic arthritis, b. active Lyme disease, c. systemic lupus erythematosus, d. infectious arthritis, e. vasculitis, f. parvovirus infection, g. rheumatoid arthritis, h. active uveitis, i. active IBD;10.Has a history of latent or active granulomatous infection, including histoplasmosis, or coccidioidomycosis, prior to Screening;11.Had a nontuberculous mycobacterial infection or opportunistic infection (e.g., cytomegalovirus, Pneumocystis jirovecii [carinii], aspergillus) within 6 months prior to Screening;12.Has a history of an infected joint prosthesis, or has received antibiotics for a suspected infection of a joint prosthesis, if that prosthesis has not been removed or replaced;13.Had a serious infection (including but not limited to, hepatitis, pneumonia, sepsis, or pyelonephritis), or has been hospitalized for an infection, or has been treated with IV antibiotics for an infection within 2 months prior to Baseline. Less serious infections (eg, acute upper respiratory tract infection, simple urinary tract infection) need not be considered exclusionary at the discretion of the investigator;14.Had a history of, or ongoing, chronic or recurrent infectious disease, including but not limited to, chronic renal infection, chronic chest infection (e.g., bronchiectasis), sinusitis, recurrent urinary tract infection (e.g., recurrent pyelonephritis, chronic nonremitting cystitis), an open, draining, or infected skin wound, or an ulcer;15.Is known to be infected with human immunodeficiency virus (HIV) or seropositive for hepatitis C virus (HCV);16.Has a chest x-ray within 2 months prior to Screening that shows an abnormality suggestive of a current active infection or malignancy;17.Has a history of lymphoproliferative disease, including lymphoma, or signs suggestive of possible lymphoproliferative disease such as lymphadenopathy of unusual size or location and/or clinically significant splenomegaly, or monoclonal gammopathy of undetermined significance;18.Has had a malignancy within 5 years before screening (exceptions are squamous and basal cell carcinomas of the skin that have been treated, with no evidence of recurrence for at least 3 months prior to Baseline; and carcinoma in situ of cervix that has been surgically cured);19.Has a history of known demyelinating diseases such as multiple sclerosis or optic neuritis;20.Has a history of or concurrent congestive heart failure ([CHF] of any grade [I IV]), including medically controlled, asymptomatic CHF;21.Has a transplanted

organ (with the exception of a corneal transplant performed >=3 months prior to baseline);22.Has current signs or symptoms of severe, progressive, or uncontrolled renal, hepatic, cardiovascular, metabolic, ophthalmological, respiratory, hematologic, gastrointestinal, endocrine, pulmonary, neurologic, psychiatric, cerebral, or other significant medical illness or disorder that, in the judgment of the investigator, could interfere with the trial, or require treatment that might interfere with the trial. Other conditions that are well controlled and stable will not prohibit participation if deemed appropriate per the investigator's judgment. ;23.Is a user of recreational or illicit drugs or has or had a substance abuse (drug or alcohol) problem within the previous 2 years;24.Has participated in any other interventional clinical trial within 30 days, inclusive, of signing the informed consent form of the current trial

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-10-2017
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Simponi
Generic name:	Golimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-05-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-07-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2015-004020-65-NL
CCMO	NL61609.056.17