A randomized, partially-blinded, active-controlled multicenter study of secukinumab to demonstrate reduction of radiographic progression versus GP2017 (adalimumab biosimilar) at 104 weeks and to assess the long term safety, tolerability and efficacy up to 2 years in patients with active ankylosing spondylitis

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The purpose of this study is to demonstrate the impact on progression of structural damage in the spine as measured by the mSASSS in patients with AS. Data from this study will be used to support the submission of an AS label extension to include a...

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

Summary

ID

NL-OMON55618

Source
ToetsingOnline

Brief title
CAIN457K2340 (SURPASS)

Condition

- Joint disorders

Synonym
ankylosing spondylitis; Bechterew□s syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: adalimumab biosimilar, ankylosing spondylitis, GP2017, secukinumab

Outcome measures

Primary outcome

Primary objective:

To demonstrate the proportion of subjects on each secukinumab dose with no radiographic progression as measured by mSASSS at Week 104 is superior to subjects on GP2017 (adalimumab biosimilar).

Secondary outcome

Secondary objectives:

1: To demonstrate the change from baseline in mSASSS in subjects on each secukinumab dose is superior to GP2017 (adalimumab biosimilar) at Week 104.

2: To demonstrate the proportion of subjects with a syndesmophyte at baseline with no new syndesmophytes at Week 104 on each secukinumab dose is superior to GP2017 (adalimumab biosimilar).

3: To evaluate the Berlin sacroiliac (SI) joint edema score in subjects on each

secukinumab dose at Week 104 versus GP2017 (adalimumab biosimilar) (in a subset of subjects at selected sites).

4: To evaluate the ASspiMRI-a Berlin modification score in subjects on each secukinumab dose at Week 104 versus GP2017 (adalimumab biosimilar) (in a subset of subjects at selected sites).

5: To evaluate ASAS 20 response, ASAS 40 response, ASAS partial remission and ASDAS inactive disease in subjects on secukinumab at Week 104.

6: Overall safety and tolerability of secukinumab.

Study description

Background summary

Ankylosing spondylitis (AS) is a chronic inflammatory disease which belongs to a group of conditions known as spondyloarthritides (SpA). It is mainly characterized by involvement of the axial skeleton and sacroiliac (SI) joints, but also affects peripheral joints, entheses and extra-articular organs. A significant proportion of patients may present with associated extra - articular manifestations such as uveitis, psoriasis, inflammatory bowel disease (IBD), cardiovascular and pulmonary abnormalities. Generalized osteoporosis, as well as regional osteopenia are common in AS patients and predispose them to non-traumatic fractures in spite of young age and gender (male). The presence of the HLA-B27 human leukocyte antigen is strongly associated with AS: 90-95% of patients with AS who have European ancestry carry this marker. AS affects up to 1.1% of the population, is associated with significant morbidity and disability, and thus constitutes a major socio-economic burden.

First-line medication of mild AS consists of non-steroidal anti-inflammatory drugs (NSAIDs). Treatment of NSAID-refractory AS is hampered by the lack of efficacy of virtually all standard disease modifying anti-rheumatic drugs (DMARDs), including methotrexate (MTX). Tumor necrosis factor (TNF) blocking agents were successfully added to the armamentarium to treat AS and subsequently demonstrated prolonged efficacy up to eight years of follow-up. However, upon discontinuation of TNF blockers the disease relapses quickly, indicating that the inflammatory process may have only been inhibited but not completely abolished.
Secukinumab, a human monoclonal antibody that inhibits the effector function of

IL-17A, has been previously shown to be better than placebo in improving the signs and symptoms of AS. In the Phase III MEASURE 1 and MEASURE 2 studies of 590 pat ients with AS, secukinumab significantly improved key clinical domains of disease versus placebo, including signs and symptoms, physical functioning, and quality of life.

Secukinumab as well as a number of anti-TNFs including adalimumab are approved for treatment of patients with active AS (Cosentyx® and Humira® package inserts and SmPCs). Results on signs and symptoms with both secukinumab and adalimumab have demonstrated good response along with rapid reduction of SI-joint and spinal inflammation as evidenced by MRI. One of the key features of AS contributing to long term disability is the process of structural remodeling in the axial skeleton and the SI-joints. This process as evidenced by SI and spinal radiography typically begins with subchondral sclerosis in the SI-joints along with squaring and marginal sclerosis of the vertebral bodies. Over time SI joint erosions occur and vertebral body syndesmophytes form, ultimately leading to spinal fusion. The process is
slow, progresses over 10 - 15 years and includes both osteoproliferative as well as absorptive processes.
Studies evaluating the effects of the anti-TNF agents adalimumab, etanercept and infliximab on radiographic damage in patients with AS did not demonstrate inhibition of radiographic progression after approximately 2 years of therapy compared to a histo rical cohort. The comparisons to the historical cohorts that had been treated with NSAIDs only have shown a mean modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) progression of 0.8 -0.9 over 2 years, regardless of anti-TNF or NSAID treatment.
Two-year spinal X-ray data from the secukinumab pivotal study MEASURE 1 suggest that IL-17A inhibition may have the potential to decrease spinal structural progression as evidenced by a mean mSASSS change after 2 years of therapy of ~ 0.3. This speaks to the potential of secukinumab to influence the long-term structural progression in the spine of patients with AS.

However, a need exists for comparative studies to assess how different mechanisms of action can reverse or slow down structural progression. This will be the first study comparing an anti-IL17A treatment with an anti-TNF agent in AS. This study will provide critical scientific evidence that will improve evidence-based decision making in the treatment of patients with AS and play an important role in filling the current data gap between clinical research and day-to-day clinical practice on the therapeutic utility of biologic therapy in patients with active AS.

Study objective

The purpose of this study is to demonstrate the impact on progression of structural damage in the spine as measured by the mSASSS in patients with AS. Data from this study will be used to support the submission of an AS label

extension to include a claim on radiographic progression.

Study design

This is a multicenter, randomized, partially-blinded, active-controlled, parallel-group study.

At baseline (BSL), approximately 837 subjects whose eligibility is confirmed will be randomized to one of three treatment groups (1:1:1).
Group 1: secukinumab 150 mg [1 x 1.0 mL s.c. plus placebo (1 x 1.0 mL s.c.)] at BSL, Weeks 1, 2 and 3, followed by administration every four weeks starting at Week 4
Group 2: secukinumab 300 mg (2 x 1.0 mL s.c.) at BSL, Weeks 1, 2 and 3, followed by administration every four weeks starting at Week 4
Group 3: GP2017 (adalimumab biosimilar) 40 mg (1 x 0.8 mL s.c.) at BSL followed by administration every two weeks

Intervention

AIN457 secukinumab
GP2017 (adalimumab biosimilar)

Study burden and risks

Burden:
Study duration: 2 * years.
15 site visits. In case IMP injections not adminstered at home, 60 site visits (GP2017) or 34 (secukinumab).
5x fasting.
Duration per visit 1 to 2 hours (in case patient visits site for IMP injection only; duration visit 15 minutes).

GP2017 group: 52 s.c. injections (biweekly)
Secukinumab group: 29 s.c. injections (every 4 weeks (1e 4 weeks; weekly))

Physical examination: approx.14x.
Blood- and urine collection: approx. ca. 15x (blood 5-30 ml)
Optional pharmacogenetic blood sample collection (6 ml): 1x
ECG at baseline
X-Ray Chest: 1x (in case not done within 3 months before start trial).
X-Ray spinal: 3x
X-Ray SI joints: 2x
MRI spinal: 4x
Completion of questionnaires (BASFI, BASDAI, ASQoL, FACIT-Fatigue, SF-36,WPAI-GH and VAS (backpain and disease activity): at 11 visits. Max duration half an hour per visit (in case VAS only: max 5 minutes).

Risk:
Side effects study medication and inconveniences study proecdures.

Contacts

Public
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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 non-pregnant, non-nursing female patients at least 18 years of age.
- Diagnosis of moderate to severe Ankylosing Spondylitis with radiologic evidence (centrally read X-ray) fulfilling the Modified New York criteria for AS despite previous or current NSAID/non biologic DMARD therapy.
- Active AS assessed by total BASDAI >= 4 on a scale of 0-10.
- Spinal pain as measured by BASDAI question #2 >= 4 (0-10).
- Total back pain as measured by visual analog scale (VAS) >= 40 mm (0-100 mm).
- hsCRP >= 5mg/L OR presence of at least 1 syndesmophyte on centrally read

spinal X-ray.

Exclusion criteria

- Patients with total ankylosis of the spine.
- Pregnant or nursing (lactating) women
- Evidence of ongoing infectious or malignant process.
- Previous exposure to any biologic immunomodulating agent, including those targeting IL-17, IL-17 receptor or TNFα.
- Subjects taking high potency opioid analgesics.
- Previous treatment with any cell-depleting therapies including but not limited to anti-CD20, investigational agents.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-01-2019
Enrollment:	26
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	biosimlar adalimumab
Generic name:	biosimlar adalimumab

Product type:	Medicine
Brand name:	Cosentyx
Generic name:	secukinumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-12-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	05-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	23-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2017-000679-10-NL
ClinicalTrials.gov	NCT03259074

Register	ID
CCMO	NL62778.018.17