A randomized, double-blind, placebo-controlled multicenter study of secukinumab 150 mg in patients with active non-radiographic axial spondyloarthritis to evaluate the safety, tolerability and efficacy up to 2 years, followed by an optimal phase of either 150 mg or 300 mg randomized dose escalation for up to another 2 years

Published: 18-02-2016
Last updated: 17-04-2024

Primary: To demonstrate the efficacy of one or both secukinumab regimens at Week 16 is superior to placebo in patients with active AS based on the proportion of patients achieving an ASAS 40 response.Secondary (key only): ASAS responses in the...

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

Summary

ID

NL-OMON47618

Source
ToetsingOnline

Brief title
CAIN457H2315 (PREVENT)

Condition

- Joint disorders

Synonym
non-radiographic spondyloartritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: non-radiografic, placebo, secukinumab, spondyloartritis

Outcome measures

Primary outcome

The proportion of TNF-naive patients achieving an ASAS 40 response

Secondary outcome

- The proportion of all patients achieving an ASAS40 response

- The proportion of TNF naïve patients achieving an ASAS40 response

- The proportion of patients meeting the ASAS 5/6 response criteria

- Change in BASDAI over time

- The proportion of patients achieving a BASDAI 50 response

- Change in hsCRP over time

- Change in BASFI over time

- Change in SI Joint Edema

- The proportion of patients achieving an ASAS20 response

- Change in SF-36 physical Component Summary over time

- Change in ASQoL over time

- The proportion of patients achieving an ASAS partial remission

- Safety and Tolerability

Study description

Background summary

The well-known ankylosing spondylitis is part of axial spodyloartritis, The form of spondyloartritis that shows no damage on X-Ray is called non-axial radiographic spondylartritis. These patients have the same symptoms and risk factors that are characteristic of axial spondylartritis. Spondyloartritis is a chronic inflammatory disease, which is mainly characterized by involvement of axial joints and bilateral sacroiliitis. It affects up to 0.9% of the population and is associated with significant morbidity and disability,and thus constitutes a major socioeconomic burden. Sometimes peripheral joints and extra-articular organs are involved as well.
Associated extra-articular manifestations include acute anterior uveitis, cardiovascular and pulmonary abnormalities, neurologic sequelae, and both clinical and subclinical gastrointestinal findings.Decreased bone mineral density is typical of extra-articular symptoms and many patients with AS have osteoporosis.
The first-line drug treatments of mild AS are NSAIDs. Treatment of NSAIDs-refractory AS is hampered by the lack of efficacy of virtually all standard disease modifying anti-rheumatic drugs including methotrexate. TNF blocking demonstrated prolonged efficacy up to three years of follow-up, but upon discontinuation of TNF blockers the disease relapses quickly. Observations so far indicate that other treatments are needed to treat patients who do not respond to
TNF-blockers and/or who have.incomplete resolution of inflammatory changes as evidenced on MRI studies.lnterleukin-17 antagonism by secukinumab represents a novel approach to interferewith ttie chronic inflammatory process.
Notably secukinumab showed good efficacy in patients with AS. This is based upon a study, in which the ASAS20 response rate at week 6 was achieved by approximately 60% of the patients.
The purpose of the present 2 year study is to demonstrate the efficacy on signs and symptoms at Week 16 and to assess the long term safety, tolerability and efficacy of secukinumab given as s.c. injections (prefilled syringes) of secukinumab versus placebo in subjects with active AS.
Secukinumab is administered as s.c. injections 150 mg (in pre-filled syringes) versus placebo in patients with active axial non-radiographic spondylarthritis.
It is the intention that the patients administer the injections themselves in

the second year if possible.
The core phase is followed by an optional 16-week extension phase that lasts for up to 2 years, but stops when the last patient has completed the first 16 weeks of this phase. During this phase it will be investigated whether a dose increase from 150 mg to 300 mg secukinumab has more benefits for patients compared to 150 mg. Long term efficacy, safety and tolerability of the 300 mg dose are investigated.

Study objective

Primary: To demonstrate the efficacy of one or both secukinumab regimens at Week 16 is superior to placebo in patients with active AS based on the proportion of patients achieving an ASAS 40 response.
Secondary (key only): ASAS responses in the subgroup and whole study population. Safety and tolerability.

Study design

Multicenter randomized double-blind phase Ill parallel-group placebo-controlled study.
Randomisation (1 :1: 1) to:
- Secukinumab 150 mg s.c. injections every 4 weeks with loading dose of one injection every week during the first month
- Secukinumab 150 mg s.c. injections every 4 weeks without loading dose (patient receives placebo during visit week 1, 2
and 3)
-Placebo , if inadequate response at week 20 secukinimab 150 mg s.c. every 4 weeks. After a year secukinumab for all placebo patients.
155 patients per treatment group. 555 patients in total.

Screening period of max. 10 weeks. Treatment period approx. 2 years. Follow-up period 8 weeks.
Evaluation of efficacy at week 16. Patients on placebo can be switched at week 20 to secukinumab if inadequate response.
Deblinding after interiim analysis week 52.

In week 104, patients can continue with an optional, randomized extension treatment with a higher dose. Patients will be assessed for their ASA20 response at week 104. Secukinumab 150 mg responders at week 104 are blind-blinded in one of the following groups:
4. Secukinumab 150 mg / placebo, every 4 weeks
5. 2 injections of Secukinumab 150 mg every 4 weeks

Patients who have not fully responded to Secukinumab at week 104 will receive a higher dose in an open-label manner:
6. 2 injections of 150 mg Secukinumab every 4 weeks (open label)

Intervention

Treatment: Secukinumab or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration appr. 2 years. 24 site visits or 33 if patients cannot inject themselves in year 2.
Year 1, visit every 4 weeks and during the first month weekly.
Year 2, visits every 12 weeks, every 4 weeks if injection takes place in the hospital.
Fasting: 9x. Average duration visit 2 hr.
29 s.c. injections every 4 weeks (1st month weekly)
Blood test 19 times, 5-30 ml each time
Optional pharmacogenetic-genomics blood test (1 0 ml)
Optional biomarkers blood test 5x (1 ml)
ECG at screening and at week 16, 52, 76 and 104
Physical examination ca 23 times
Chest X-Ray: 2x
X-Ray cervical, thoracal and lumbal spine: 2x
X-Ray Sacro iliiacal joint: 2x
TBC skin test: 1x
Visual analogue scales: Diseases activity, pain, BASFI, BASDAI, EQ-5D, FACIT-Fatigue, SF-36, WPAI-GH; Per visit 3-7
questionnaires (plus 2x 1 VAS): Once every 1-3 months.

Extension phase (maximum burden)
Duration: maximum 2 years and 11 visits, on average 2 hours per visit
26 s.c. injections every 4 weeks
Physical examination: 9x
Questionnaires: 5x
Blood collection for lab determinations: 9x
Pregnancy test (if applicable): 9x

Contacts

Public
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Scientific

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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 axSpA according to ASAS axSpA criteria
• Objective signs of inflammation (MRI or abnormal CRP)
• Active axSpA as assessed by total BASDAI >=4 cm
• Spinal pain as measured by BASDAI question #2 >= 4 cm (0-10 cm) at baseline
• Total back pain as measured by VAS >= 40 mm (0-100 mm) at baseline
• Patients should have been on at least 2 different NSAIDs with an inadequate response
• Patients who have been on a TNFα inhibitor (not more than one) must have experienced an inadequate response
For the extension phase of the study:
• Patients who have completed the full study treatment period (104 weeks) in the core phase on study treatment.
• Other protocol-defined inclusion criteria may apply

Exclusion criteria

• Patients with radiographic evidence for sacroiliitis, grade >= 2 bilaterally or grade >= 3 unilaterally
• Inability or unwillingness to undergo MRI
• Chest X-ray or MRI with evidence of ongoing infectious or malignant process

• Patients taking high potency opioid analgesics
• Previous exposure to secukinumab or any other biologic drug directly targeting IL-17 or IL-17 receptor
• Pregnant or nursing (lactating) women
• Other protocol-defined exclusion criteria may apply

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):	09-08-2016
Enrollment:	12
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	18-02-2016

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-06-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-12-2019

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	EUCTR2015-001106-33-NL
ClinicalTrials.gov	NCT02696031
CCMO	NL56103.018.16