A randomized, double-blind, placebo-controlled phase III multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate the efficacy at 16 weeks and to assess the long-term efficacy, safety and tolerability up to 5 years in patients with active Ankylosing Spondylitis (CAIN457F2310)

Published: 16-08-2012
Last updated: 26-04-2024

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 20 response in the subgroup of patients who are TNF*...

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

Summary

ID

NL-OMON43926

Source
ToetsingOnline

Brief title
CAIN457F2310

Condition

- Joint disorders

Synonym
ankylosing spondylitis

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: ankylosing spondylitis, placebo, secukinumab

Outcome measures

Primary outcome

ASAS20.

Secondary outcome

ASAS20, ASAS40, adverse events.

Study description

Background summary

Ankylosing spondylitis (AS) 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.
Interleukin-17 antagonism by secukinumab represents a novel approach to interfere with the chronic inflammatory process. Notably secukinumab showed good efficacy in patients with AS. This is based upon an interim analysis of the ongoing Proof of Concept study, in which the ASAS20 response rate at week 6 was achieved by approximately 60% of the patients.
The purpose of the present 5 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 2 dose levels of secukinumab versus placebo in subjects with active AS.

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 20 response in the subgroup of patients who are TNF* inhibitor naïve.
Secondary (key only): ASAS20 week 16 response in the whole study population. ASAS40 week 16 response in the subgroup and whole study population. Safety and tolerability.

Study design

Multicenter randomized double-blind phase III parallel-group placebo-controlled study.
Randomisation (1:1:1) to:
* Secukinumab 75 mg (s.c. injections every 4 weeks) *)
* Secukinumab 150 mg (s.c. injections every 4 weeks) *)
* Placebo.
*) after loading period of 4 week with weekly injections.
Screening period of max. 10 weeks. Treatment period approx. 5 years. Follow-up period 12 weeks.
Evaluation of efficacy at week 16. Patients on placebo will be switched at week 16 to secukinumab (randomized allocation of dose (75 or 150 mg secukinumab).
After Interim Analysis week 52 data: Unblinding; open-label treatment (75 of 150 mg secukinumab).
After approval protocol version 02: Possibility to increase dose form 75 mg to 150 mg secukinumab if therapeutic response is not fully achieved with the current dose of 75 mg and may improve with a higher dose (judged by investgator).

Independent DSMB.

Approx. 220 patients.

Intervention

Until week 16: treatment with secukinumab (75 of 150 mg) or placebo, doubleblind.
As of week 16: treatment with secukinumab (75 of 150 mg), doubleblind.
After interim analysis week 52 data: Treatment secukinumab (75 of 150 mg), open-label.
After approval protocol version 02: Possibility to increase dose form 75 mg to 150 mg secukinumab if therapeutic response is not fully achieved with the current dose of 75 mg and may improve with a higher dose (judged by investgator).

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration approx. 5 years. Approx. 44 visits: every 4 weeks (1st 4 visits 1 week apart) during year 1-2, every 12-16 week during year 3-5. Fasting 13x. Duration 2-3 h.
Approx. 85 s.c. injections every 4 weeks (1st 4 weeks: weekly).
Physical examination approx. 35 times.
Blood tests approx. 35 times, 5-30 ml/occasion.
Optional pharmacogenetic/-genomics blood test (10 ml).
ECG every 6 months.
TBC skin test 1x.
Chest X ray 1x (if not performed in previous 3 months).
Visual analogue scales: disease 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.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6834 DP
NL
Scientific
Novartis

Raapopseweg 1

Arnhem 6834 DP
NL

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-lactating female patients at least 18 years of age.
* Diagnosis of moderate to severe AS with prior documented radiologic evidence (X-ray) fulfilling the Modified New York criteria for AS.
* Patients should have been on NSAIDs with an inadequate response.
* Patients who are regularly taking NSAIDs as part of their AS therapy are required to be on a stable dose for at least 2 weeks.
* Patients who have been on an anti-TNF* agent (not more than one) must have experienced an inadequate response.

Exclusion criteria

* Chest X-ray with evidence of ongoing infectious or malignant process.
* Previous exposure to secukinumab or any other biologic drug directly targeting IL-17 or IL-17-receptor.
* Patients previously treated with any biological immunomodulating agents except for those targeting TNF*
* Previous treatment with any cell-depleting therapies

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):	27-11-2012
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2016
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:	27-07-2016
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:	22-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2017
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

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	EUCTR2012-000046-35-NL
ClinicalTrials.gov	NCT01649375
CCMO	NL41490.018.12