A randomized, double-blind, placebo-controlled, multicenter study of secukinumab to demonstrate the efficacy at 16 weeks and to assess the long term safety, tolerability and efficacy up to 2 years in patients with active Ankylosing Spondylitis

Published: 29-07-2011
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Primary: To demonstrate the efficacy of each secukinumab regimen 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 TNFα inhibitor naïve.…

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

Summary

ID

NL-OMON36106

Source
ToetsingOnline

Brief title
CAIN457F2305

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 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 on signs, symptoms and spine structure of secukinumab given as i.v. loading doses, followed by s.c. injections of 2 dose levels of secukinumab versus placebo in subjects with active AS despite current or previous NSAID, DMARD and/or anti-TNF therapy.

Study objective

Primary: To demonstrate the efficacy of each secukinumab regimen 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 TNFα 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 i.v. loading doses of 10 mg/kg at baseline, week 2 and 4.
Screening period of max. 4 weeks. Treatment period approx. 2 years.
Evaluation of efficacy at week 16. Patients on placebo, who do not show improvement, will be switched at week 16 to secukinumab (randomized allocation of dose). Patients who have shown a reaction, will continue placebo treatment until week 24 and will be switched at that time point.
Unblinded local pharmacist.
Independent DSMB.
An interim analysis will be performed after all subjects have completed the Week 52 visit.
Approx. 350 patients.
After study ends, possibility to enter an follow-up study.

Intervention

Treatment with Secukinumab or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration approx. 2 years. Approx. 30 visits: every 4 weeks (1st 4 visits 1-2 weeks apart). Fasting 7x. Duration 2-3 h.
3x i.v. infusion study medication (loading doses, 150 ml in 30 min), subsequently s.c. injections every 4 weeks.
Physical examination 1st year every visit, 2nd year every 2nd visit.
Blood tests 1st 6 months every visit, thereafter every 2nd visit, 5-15 ml/occasion.
Optional pharmacogenetic/-genomics blood test (10 ml).
Pregnancy test (if relevant) every 4-12 weeks.
ECG 5x.
TBC skin test 1x.
Chest X ray 1x.
X rays spine: 2x.
DEXA scan 3x.
MRI scan (subset of patients) 3x.
Visual analogue scales disease activity and pain, ASQoL, BASFI, BASDAI, EQ-5D, FACIT-Fatigue, SF-36, WPAI-GH. Per occasion 3-7 questionnaires (plus 2x 1 VAS). 1st 6 months every 4-8 weeks, thereafter end of year 1 and 2.

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

• 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 (1984)
• 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
• Patients who have been on an anti-TNFα agent (not more than one) must have experienced an inadequate response
Other protocol-defined inclusion criteria may apply.

Exclusion criteria

• Chest X-ray with evidence of ongoing infectious or malignant process
• Patients with total ankylosis of the spine
• Patients previously treated with any biological immunomodulating agents except for those targeting TNFα
• Previous treatment with any cell-depleting therapies
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):	24-11-2011
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	secukinumab
Generic name:	secukinumab

Ethics review

Approved WMO Date:	29-07-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-02-2013
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:	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:	14-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2014
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
Other	clinicaltrials.gov, registratienummer n.n.b.
EudraCT	EUCTR2010-024529-18-NL
CCMO	NL37069.018.11