A randomized, double-blind, placebo-controlled, phase III multicenter study of subcutaneous secukinumab (150 mg) with and without a subcutaneous loading regimen to assess efficacy, safety, and tolerability up to 2 years in patients with active ankylosing spondylitis

Published: 10-02-2015
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON44029

Source
ToetsingOnline

Brief title
MEASURE 4

Condition

- Joint disorders

Synonym
Bechterew disease

Research involving
Human

Sponsors and support

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

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 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.

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.
Secondary (key only): ASAS40 week 16 response 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 until week 16, secukinimab 150 mg s.c. every 4 weeks after week 16

108 patients per treatment group.
Screening period of max. 10 weeks. Treatment period approx. 2 years. Follow-up period 12 weeks.
Evaluation of efficacy at week 16. Patients on placebo will be switched at week 16 to secukinumab

Deblinding after interiim analysis week 52.

Intervention

Treatment: Secukinumab or placebo.

Study burden and risks

Risk: Adverse effects of study medication.

Burden: Study duration appr. 2 years 23 site visits or 32 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
29 s.c. injections every 4 weeks (1st month weekly)
Bloodtest 19 times, 5-30 ml each time
Optional pharmacogenetic / genomics blood test (10 ml)
ECG at screening, after 16, 52, 76 and 104 weeks
Physical examination 23 times
Chest XRay 2 time
TBC skin test: 1 time
Visual analogue scales: Diseases activity, pain, BASFI, BASDAI, EQ-5D, FACJT-Fatigue, SF-36, WPAI-GH; Per visit 3-7
questionnaires (plus 2x 1 VAS): Once every 1-3 months.

Contacts

Public
Novartis

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Scientific
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Moderate to severe AS
- Prior radiographic evidence according to the Modified NY Criteria (1984)
- Inadequate response to NSAIDs;See protocol for other inclusion criteria.

Exclusion criteria

- Pregnancy or lactation
- On-going infectious or malignant process on a chest X-ray or MRI
- Previous exposure to IL-17 or IL-17R targeting therapies
- Previous exposure to any biological immunomodulating agent excluding TNF antagonists
- Previous cell depleting therapy;See protocol for other exclusion criteria.

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):	04-06-2015
Enrollment:	15
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:	10-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2015
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:	14-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2015
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2016
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	EUCTR2013-005575-41-NL
ClinicalTrials.gov	NCT021590053
CCMO	NL51847.018.15