A randomized, double-blind, placebocontrolled, 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 Last updated: 14-04-2024

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. Secondary (key only): ASAS40 week 16 response in...

Ethical review Approved WMO **Status** Recruitment stopped

Health condition type Joint disorders **Study type** Interventional

Summary

ID

NL-OMON44029

Source

ToetsingOnline

Brief titleMEASURE 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 III 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.

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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

Raapopseweg 1 Arnhem 6824 DP

NL

Scientific

Novartis

Raapopseweg 1 Arnhem 6824 DP NL

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

EudraCT ClinicalTrials.gov CCMO ID

EUCTR2013-005575-41-NL NCT021590053 NL51847.018.15