A randomized, double-blind, placebo-controlled, parallel group, Phase II, 24-week study investigating the efficacy, safety and tolerability of AIN457 in patients with active overuse tendinopathy refractory to oral NSAIDs/acetaminophen, physiotherapy or corticosteroid injections

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To assess the efficacy of secukinumab 300 mg s .c. vs. placebo in patients with overuse rotator cuff tendinopathy in relieving clinical symptoms at week 14

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

Summary

ID

NL-OMON44187

Source
ToetsingOnline

Brief title
Efficacy of AIN457 with active overuse tendinopathy

Condition

- Joint disorders

Synonym

Rotator-cuff tendinopathy, shoulder pain

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AIN457, IL-17A-Ab, Overuse Tendinopathy, Rotator Cuff, Shoulder

Outcome measures

Primary outcome

The Western Ontario Rotator Cuff (WORC) patient reported outcome (PRO) score at

week 14

Secondary outcome

* WORC score at Weeks 2, 4, 8, 12, 18 and 24

* Disability of Arm, Shoulder and Hand Questionnaire (QuickDASH) score at Weeks

2, 4, 8, 12, 14, 18 and 24

* American Shoulder and Elbow Surgeons Shoulder Evaluation Form (ASES) score at

Weeks 2, 4, 8, 12, 14, 18 and 24

* EQ5D-3L score at Weeks 2, 4, 8, 12, 14, 18 and 24

* Pain score using a VAS scale (considering the last 24 hours) at Weeks 2, 4,

8, 12, 14, 18 and 24

* Patient global assessment (PGA) score using a VAS scale (considering the last

24 hours), at Weeks 2, 4, 8, 12, 14, 18 and 24

* Physician global assessment (PhGA) score using a VAS scale (considering the

last 24 hours), at Weeks 2, 4, 8, 12, 14, 18 and 24

* MRI Sein score at Weeks 8, 14 and 24

* PK/immunogenicity assessment at Day 1, Weeks 4, 12, 24

* Safety and tolerability assessments over time: Incidence and severity of AEs

and SAEs; routine safety laboratory parameters

Study description

Background summary

Overuse tendinopathy is a complex multi-faceted disease of the tendon, clinically diagnosed after gradual onset of activity-related pain, decreased function and sometimes with localized swelling of the tendon (Riley 2005, Riley 2008). Historically the terms *tendinitis* and *tendinosis* have interchanged with the term *tendinopathy*, however, these definitions are now included in the spectrum of human tendon disorders (*tendinopathy*). Tendinopathy is a common overuse injury in the athletic and working populations; it is the most common reason for consultation for a musculoskeletal complaint, corresponding to around 30% of all such consultations with a general practitioner (Forde et al 2005; Riley 2008). The exact incidence of overuse tendon injuries is not known, but in sports medicine, they account for 30% to 50% of all injuries (Scott and Ashe 2006). Generally, for physical workers, the prevalence of musculoskeletal symptoms increases with duration of employment (Forde et al 2005).

Study objective

To assess the efficacy of secukinumab 300 mg s .c. vs. placebo in patients with overuse rotator cuff tendinopathy in relieving clinical symptoms at week 14

Study design

This is a randomized, double-blind, placebo-controlled, multi-center, Phase II study of s.c. secukinumab 300 mg in approximately 100 randomized patients with overuse rotator-cuff tendinopathy without systemic inflammatory disease and refractory to NSAIDs/acetaminophen, physiotherapy or corticosteroids.
The patient and investigator will be blinded throughout the study, while the sponsor will be blinded until after the analysis of the primary endpoint.
The study consists of a 4-week screening period, a 2-week run-in period, a 12-week treatment period and a 12-week follow-up period after last treatment.

Intervention

Group 1: Secukinumab 300 mg s.c. (2 x 150 mg)
Group 2: Placebo s.c. (2 injections)

Study burden and risks

It is anticipated that secukinumab will have a beneficial effect on the symptoms of rotator cuff tendinopathy, by inhibiting the IL-17 driven inflammation and thereby decreasing pain and improving mobility and sleep. Ultimately, this should result in few cases of tendinopathy progressing to a tear and therefor lessen the need for surgery.
The placebo patients in the study will not have this benefit, however, they will be followed closely in order to identify any progress or need for additional therapy.
The risk to subjects in this trial will be minimized by compliance with the eligibility criteria, close clinical monitoring and extensive guidance to the investigators, provided in the current version of the Investigator*s Brochure (IB).

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

Patients eligible for inclusion in this study must fulfill all of the following criteria:
* Written informed consent obtained prior to all study specific screening procedures, as close to the start of the screening period as possible
* Male or non-pregnant, non-lactating female patients 18 to 65 years of age at randomization
* Presence of unilateral rotator cuff tendinopathy with:
a. Symptoms present *6 weeks, but <12 months prior to randomization
b. Tendinopathy with no more than a 50% tear as established by ultrasound at screening and MRI at baseline: Sein MRI tendinopathy scoring system grade I-III; with no tear or partial tear [maximum 50% tendon thickness (Bauer tendon thickness score maximum 2); AP length maximum 10 mm (Bauer tendon length score max 2)]. Maximum 50% of patients with partial tear
c. Pain in the affected shoulder (at rest or on movement) on at least 3 days out of 7 days in the past week prior to baseline and a score of *4 out of 10 on a VAS pain scale
d. Positive *Painful Arc Test* on examination and/or nightly pain in the affected shoulder on at least 4 out of 7 days in the past week prior to baseline
* The rotator-cuff tendinopathy must have been refractory to standard treatment defined as:
- NSAIDs / acetaminophen
- In the run-in period patients should be on a stable dose of NSAIDs and/or acetaminophen for at least 2 weeks prior to randomization, not exceeding * e.g.: Ibuprofen 1600 mg/d, naproxen 1000 mg, diclofenac 105 mg/d, or diclofenac sodium enteric-coated tablets 150 mg/d, or equivalent.
- If patients cannot tolerate these doses, the maximal tolerable dose should be used, and may be augmented with acetaminophen/paracetamol, at doses not exceed local guidelines or 4 g/day, whichever is lower. This medication should also be at a stable dose for at least 2 weeks.
- If patients have contraindications to NSAIDs or to acetaminophen, these treatments can be omitted (contraindication, drug and dose must be specified in the eCRF).
- If patients were refractory to at least 2 weeks of previous treatment as specified in 4 i/ii, NSAIDs or acetaminophen treatment can be omitted.
* Physiotherapy
- In the run in period patients should have had 2 weeks of a standardized physiotherapy treatment before randomization

Exclusion criteria

* History of hypersensitivity to any of the study treatments or excipients or to drugs of similar chemical classes
* Rheumatologic, inflammatory diseases, including but not limited to: PsA, AS and RA
* Previous shoulder surgery in affected shoulder
* History of adhesive capsulitis/frozen shoulder or calcification in the tendon (in affected or contralateral shoulder) confirmed by X-Ray, historic X-Rays can be used if performed within 3 months of baseline
* Symptomatic osteoarthritis of the shoulder (gleno-humeral, acromioclavicular) (in affected or contralateral shoulder confirmed by X-Ray, historic X-Rays can be used if performed within 3 months of baseline
* Neck conditions, including but not limited to cervical spine syndrome, which in the opinion of the investigator, may explain the patient*s symptoms
* Previous platelet rich plasma injections within the last 12 months prior to randomization

Study design

Design

Study phase:	2
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):	24-10-2017
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AIN457
Generic name:	Secukinumab

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-09-2019
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2017□003099□30-NL
CCMO	NL63318.056.17