Mechanism of action study of anti-IL17 therapy in spondyloarthritis: impact on cellular and molecular pathways of synovial inflammation and tissue remodelling.

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To assess the efect of IL-17 blockade on:- the global synovial histology and inflammatory infiltration- the number and type of IL-17 producing cells in SpA synovitis- the productuion of inflammatory mediators (including other IL-17 related cytokines...

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

Summary

ID

NL-OMON41538

Source
ToetsingOnline

Brief title
MoA IL-17 in Spondyloarthritis

Condition

- Autoimmune disorders
- Joint disorders

Synonym
ankylosing spondylitis, Spondylarthropathy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: collectebussen,Novartis

Intervention

Keyword: Anti IL-17 therapy, Mechanism of action, Spondyloarthritis, Synovial biopsies

Outcome measures

Primary outcome

- Changes in the synovial cellular and molecular pathways as indicated in the objectives between baseline and week 12

Secondary outcome

- Stratification of these cellular and molecular changes according to the genetic biomarkers of relevance for anti-IL17 treatment response
- Correlation between the synovial features at baseline and the clinical response at week 12
- Comparison of the synovial molecular changes induced by anti-IL17 with the changes induced by anti-TNF (historical samples in a similar patient population and study setting)
- Comparison of the changes in Target to Background Ration (TBR) as an indicator of vessel wall inflammation assessed by FDG PET/CT of the aorta and carotid arteries

Study description

Background summary

Spondyloarthritis is the second most frequent form of chronic inflammatory

arhtritis with a prevalence of 0.5%. It effects mainly young adults and leads to major functional handicap due to inflammation of axial and peripheral joints as well as progressive ankylosis and structural damage.
In the late nineties we introduced TNF blockade as a successfull treatment, but: only 50% responds well and tolerates, antiTNF does not halt the structural damage and TNF blockade does no induce long lasting remission as almost all patients relapse within a few weeks after interruption of the treatment. There is thus a high unmet need for alternatives.

The rationale for anti-IL17 therapy is based on various auto-inflammatory and auto immune models, preliminary efficacy data in psoriasis and RA and an association of SpA with IL23R SNPs.

Preliminary efficacy data on anti-IL17 shows that it is a highly effective treatment for signs and symptoms in SpA, moreover sub-analysis of the anti-TNF naïve patients shows the same trend.

Study objective

To assess the efect of IL-17 blockade on:
- the global synovial histology and inflammatory infiltration
- the number and type of IL-17 producing cells in SpA synovitis
- the productuion of inflammatory mediators (including other IL-17 related cytokines and TNF) and total tissue biopsies (ex vivo culture system)
- The synovial stromal cell signature
- The pan-genomic synovial gene expression profile
Secondary:
To compare wich molecular disease pathways are affected by IL-17 blockade and not by TNF blockade and thereby identify molecular biomarkers which may help to determine which patients may benefit form this treament in comparison with anti-TNF treatment.
To assess wether AIN457 sileces vessel wall inflammation (by means of 18F-FDG PET/CT of the carotic arteries and aorta.

Study design

Single centre, 12-week open label study in subjects with clinically active peripheral spondylarthritis, with open label extension up to 2 years. Synovial biopsies and FDG PET/CT of the aorta and carotid arteries will be obtained from patients before and after 12 weeks of treatment with secukinumab.

Intervention

Secukinumab (AIN457) by monthly subcutanious injections.

Study burden and risks

Medium risk

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 females age 18-70
- Diagnosis of SpA according to ESSG criteria and/or ASAS criteria
- Active disease defined by *1 swollend and * 1 tender joint, and at least 1 swollen knee or ankle joint at baseline

Exclusion criteria

- Evidence for infectious or malignant process (on chest X ray/MRI etc)
- Pts taking opioid angalgetics
- Previous IL-17 therapy exposure
- Previous use of celldepleting therapies, biological immunomodulants (except for a.TNF)
- no more then 50% of included patients are allowed to be previously exposed to (1) TNF blocking agent
- Significant medical problems or diseases

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	07-01-2014
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-02-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2015
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	EUCTR2013-002709-79-NL
CCMO	NL45246.018.13