A Stratification trial to determine key immunological factors predicting Tofacitinib efficacy in Psoriatic Arthritis (PsA). TOFA-PREDICT

Published: 25-01-2018
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This study has been transitioned to CTIS with ID 2024-510903-12-00 check the CTIS register for the current data. Primary objective:Identify pre-treatment profiles with integrated clinical, transcriptomic, metabolomic, proteomic, flow cytometric, and…

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

Summary

ID

NL-OMON54653

Source
ToetsingOnline

Brief title
TOFA-PREDICT

Condition

- Joint disorders

Synonym
psoriatic arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Pfizer

Intervention

Keyword: Psoriatic arthritis, tofacitinib

Outcome measures

Primary outcome

Main study parameters/endpoints:

-Minimal Disease Activity (MDA) at week 16

-Baseline molecular network profile (based on the composite systems medicine analysis)

Secondary outcome

-change (50%) in the molecular network before treatment as compared to after (week 4 and 16) treatment

-change in composite clinical disease activity scores (MDA, ACR(20,50,70) response, DAS28) at week 16.

-change in individual clinical parameters that make up the composite scores (i.e. PASI score (reduction of 50%, 75%, 90%), joint count, CRP, ESR, QOL-measures) at week 16

Study description

Background summary

Rationale: Psoriatic arthritis is currently treated by an array of drugs, yet the best choice of drug for the individual patient in both the early phase of the disease and the later phase of disease is unknown. As a consequence, patients undergo a *trial and error* approach to treatments, delaying time to treatment response and negatively impacting quality of life.

Study objective

This study has been transitioned to CTIS with ID 2024-510903-12-00 check the CTIS register for the current data.

Primary objective:
Identify pre-treatment profiles with integrated clinical, transcriptomic, metabolomic, proteomic, flow cytometric, and imaging data that predict response to treatment with tofacitinib, in DMARD-naïve and DMARD non-responsive PsA patients.

Secondary objectives:
- Compare clinical efficacy of treatment with tofacitinib, methotrexate and etanercept in DMARD-naïve and DMARD-non responsive patients with active PsA
- Determine (medication specific) molecular mechanisms predicting and underlying clinical response to tofacitinib in comparison to methotrexate and etanercept in active PsA

Study design

Study design: Multicentre, open label, randomized phase III clinical trial in active psoriatic arthritis patients. In arm 1, patients are naïve to csDMARD and will be randomized to receive either methotrexate monotherapy or tofacitinib monotherapy. In arm 2, patients are being treated with methotrexate background therapy yet still have active disease and will be randomized to receive additional etanercept or additional tofacitinib. Treatment failure will result in therapy switch (combination therapy in Arm1; cross-over in Arm2). Biological studies will be performed throughout the study.

Intervention

Intervention (if applicable):
-Treatment with either standard of care drugs (methotrexate, etanercept) or the phase III interventional study drug tofacitinib (orally, 5mg twice per day)

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
-Imaging studies (MRI, PET-CT, X-rays), low risk
-Venapuncture (3x), low risk
-Clinical examinations and questionnaires (BL,4, and 16 weeks), low burden
-Therapeutic intervention with either standard of care (methotrexate or etanercept) or the interventional study drug (tofacitinib): moderate 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

• Age 18-75 years old
• Meets CASPAR criteria for psoriatic arthritis
• Disease duration of at least 8 weeks
• Evidence of active arthritis based upon >=2 swollen joints and >=2 tender joints
• Subjects are to discontinue active psoriasis treatment prior to being enrolled in the study.
• Inclusion criteria arm 1:
o No history of csDMARD use or bDMARD therapy use
• Inclusion criteria arm 2:
o Current use of methotrexate, sulfasalazine or leflunomide on the highest tolerated dosage and on a stable dosage for at least 4 weeks prior to randomization. Highest dosage accepted respectively are max <=25mg/wk, 20mg/day

and 3000mg/day.
o *History of use of max. 1 bDMARD prior to inclusion is allowed, except:
- Prior use of etanercept
- Primary failure (total non-response at start) on other TNFi (adalimumab, golimumab, infliximab, certolizumab). Patients that have had a loss of response on their first TNFi are allowed to participate.
o No history of tsDMARD therapy use (JAKi, abatacept)

Exclusion criteria

• Currently have pustular psoriasis only
• Participation in other studies involving investigational drug(s) (Phases 1-4) within 4 weeks before the current study begins and/or during study participation. Participation in any observational studies during study participation.
• Pregnant females, breastfeeding females, females of child-bearing potential not using highly effective contraception or not agreeing to continue highly effective contraception for at least one ovulatory cycle after last dose of investigational product or females planning pregnancy. Women of childbearing potential must test negative for pregnancy prior to enrolment in this study.
• Current or recent history of a severe, progressive or uncontrolled renal, hepatic, hematological, gastrointestinal, metabolic (including hypercholersterolemia), endocrine, pulmonary, cardiovascular, or neurologic disease.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-05-2018
Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Enbrel
Generic name:	Etanercept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	methotrexaat
Generic name:	methotrexaat
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xeljanz
Generic name:	Tofacitinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-01-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-04-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-07-2018

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-12-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-05-2022

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-05-2024
Application type:	Amendment
Review commission:	METC NedMec

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
EU-CTR	CTIS2024-510903-12-00
EudraCT	EUCTR2017-003900-28-NL
CCMO	NL63439.041.17