Clinical effectiveness of 2 treat to target strategies, mimicking standard care compared to early secukinumab for the treatment of Moderate to Severe Psoriatic arthritis: a parallel group randomised controlled trial.

Published: 08-07-2019
Last updated: 14-12-2024

Primary Objective: To compare the effectiveness of the administration of secukinumab to standard care in newly diagnosed Psoriatic Arthritis patients on the ACR50 response at 6 months. Secondary Objectives: To compare effectiveness at 6 and 12…

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

Summary

ID

NL-OMON55356

Source
ToetsingOnline

Brief title
STAMP

Condition

- Autoimmune disorders
- Synovial and bursal disorders
- Epidermal and dermal conditions

Synonym
psoriatic arthritis; Joint inflammation affecting individuals with the skin disorder psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Novartis

Intervention

Keyword: Psoriatic Arthritis, Secukinumab, Treatment strategies, Usual care

Outcome measures

Primary outcome

The ACR50 response will be used to determine efficacy at 6 months. A subject is defined as an ACR50 responder if, and only if, the following three conditions are met:

1. they have a >= 50% improvement in the number of tender joints (based on 68 joints)

2. they have a >= 50% improvement in the number of swollen joints (based on 66 joints)

3. they have a >= 50% improvement in three of the following five domains:

- Patient*s global assessment of disease activity (measured on a VAS scale, 0-100)

- Physician*s global assessment of disease activity (measured on a VAS scale, 0-100)

- Patient*s assessment of PsA pain (measured on a VAS scale, 0-100)

- Health Assessment Questionnaire - Disability Index (HAQ-DI©) score

- Acute phase reactant (hsCRP or ESR)

Secondary outcome

- ACR20 and ACR70 at 6 months;

- ACR20/50/70 at 12 months;

- MDA (The proportion of subjects achieving minimal disease activity, which is defined as 5 of the following 7 domains: <= 1 tender joint count, <= 1 swollen joint count, PASI <= 1 or BSA<=3%, patient pain VAS <= 15, patient global assessment of disease activity VAS <= 20, HAQ-DI© <= 0.5, tender entheseal points <= 1) at 12 months

- VLDA (Very Low Disease Activity), DAPSA (Disease Activity in PSoriatic Arthritis) and PASDAS (Psoriatic Arthritis Disease Activity Score) at 6 and 12 months;

- SF-36 (36-item, patient-reported survey of patient health), BRAF (Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire) and PSAID (Psoriatic Arthritis Impact of Disease Questionnaire) at 12 months;

- PCQ (Psychological Capital Questionnaire) at 12 months;

- The PsA-modified Sharp/van der Heijde score (SHS) at 12 months.

Study description

Background summary

Psoriatic Arthritis (PsA) is a chronic inflammatory joint disease with an estimated prevalence of 0.5% in the general population. It manifests in skin, joints, enthesis and spine and when left untreated results in joint damage, structural changes in the enthesis and spine. Moreover, it can have a dramatic impact on the quality of life. Over recent years treatment options are vastly expanding.

With more emergent effective treatments for inflammatory arthritis, the concept of treat-to-target is growing to its full potential. In rheumatoid arthritis (RA), this treatment approach has been proven to be effective, leading to less erosive progression, more drug free remission and better quality of life. Treat to target is a treatment strategy in which treatment is optimized to reach and maintain explicitly specified goals, such as remission or low disease activity.

In PsA, the treat to target principle is less often applied and has only been studied by Coates et al. The TICOPA study used a step-up approach in the tight control arm. Patients were started on methotrexate, sulfasalazine and subsequently a TNF blocker was added if patients did not meet the pre-specified target of Minimal Disease Activity (MDA). Patients in the tight control group had a higher chance (odds) of achieving an ACR-20 response than the standard care group (odds ratio 1·91, 95% CI 1·03-3·55; p=0·04). ACR50, ACR70, and PASI75 responses were also achieved more frequently in the tight control group than in the standard care group. However, there was little difference for resolvement of dactylitis and enthesitis in the tight control group as compared to the standard care group, and there was no difference in damage progression. This indicates that a treat to target approach is feasible in the treatment of PsA, but not all disease features responded well on the TICOPA regime suggesting that better treatment strategies are needed.

Studies in patients with RA established that early aggressive treatment in a treat to target strategy improves outcome. For instance, in the BEST study and the TREACH study combination therapy arms outperformed the mono therapy arms on joint damage and drug free remission. However, up to date there is ample to no data on early aggressive treat to target treatment in PsA.

The initial drug used in the TICOPA trial was methotrexate. Methotrexate is a controversial drug in the treatment of PsA. The effect on skin psoriasis has been proven extensively, however there is little to no evidence for the efficacy of methotrexate in PsA treatment. Despite this drug being generally regarded and reflected in guidelines as first line treatment for the arthritis component of PsA, this is not the case for its effect on inflammatory backpain, enthesitis or dactylitis. This implicates that early strategies using treatment covering all PsA disease features could improve outcome.

Over the past couple of years, therapeutic targets for treatment of PsA are rapidly evolving. Interleukine-17a blockade (e.g. secukinumab) is one of the evolving treatments and plays an important role in the pathophysiology of PsA. In contrast to methotrexate, in clinical setting it is beneficial on all the effected sites in patients with PsA. It also significantly improves patient reported outcome measures. We hypothesize that treatments covering all features of PsA by early aggressive therapeutic intervention, using secukinumab as an initial treatment strategy will improve treat to target in PsA.

Study objective

Primary Objective:
To compare the effectiveness of the administration of secukinumab to standard care in newly diagnosed Psoriatic Arthritis patients on the ACR50 response at 6 months.

Secondary Objectives:
To compare effectiveness at 6 and 12 months between two treatment arms, mimicking standard care (arm 1) and early secukinumab arm (arm 2) using:
- Patients achieving ACR 20 and 70 at 6 months
- Patients achieving ACR 20, 50, 70 at 12 months
- Patients achieving MDA and VLDA at 6 and 12 months
- DAPSA and PASDAS scores at 6 and 12 months

To compare Quality of life at 12 months between two treatment arms, mimicking standard care (arm 1) and early secukinumab arm (arm 2) using:
- SF36
- PSAID
- BRAF

To compare work performance (presenteeism and absenteeism) at 12 months between between two treatment arms, mimicking standard care (arm 1) and early secukinumab arm (arm 2)

To compare progression of radiological damage at 12 months between two treatment arms, mimicking standard care (arm 1) and early secukinumab arm (arm 2) using:
- PsA modified Sharp vd Heijde (SHS) at 12 months

To assess the cost-effectiveness between two treatment arms, mimicking standard care (arm 1) and early secukinumab arm (arm 2).

Study design

The DEPAR-t2t trial is designed as a randomized, controlled, parallel group, open label, multi-center comparing two treat-to-target strategies within a cohort.
Arm 1: Mimicking standard care. The standard care is based on data from the DEPAR cohort and interviews with Dutch rheumatologists.
Arm 2: Secukinumab 300 mg
Therapy in each arm will be escalated using a 3 monthly scheme in patients not achieving the treatment target (MDA).

For this research we will use a Trials Within Cohorts (TWiCs) design. This method recruits a central cohort having *treatment as usual* with regular

observations and then adds pragmatic trials of alternative therapies in which a random group of eligible patients are selected. This allows robust generalizability from studies to routine health care, avoids attrition and disappointment bias from controls in open label studies as patients receive only information relevant to their care, aids recruitment to trials, allows routine collection of long term outcomes and increases efficiency with multiple trials within one cohort. The currently running DEPAR cohort will function as the central cohort. Patients fulfilling the inclusion criteria for the treat to target trial will be offered to participate in the study. Patients refusing aforementioned will remain in the central cohort.

Patients diagnosed by the rheumatologist and fulfilling the CASPAR criteria for Psoriatic Arthritis will be eligible if they present with oligo-arthritis (2 to 5 involved joints) or with poly-arthritis (5 or more joints).

Participants in this study will attend for study visits at baseline and months 3, 6, 9 and 12. After 6 weeks patients will be asked to fill out 5 questionnaires. At the 3-monthly visits, participants will be assessed clinically for disease activity and will be asked to complete patient reported outcomes via questionnaires. Visits in between these will be performed based on clinical need when adjustment to therapy is required.
Based on the evaluations, MDA will be calculated and therapy will be escalated or continued

Intervention

This is a 2-arm strategy study.

ARM 1: Mimicking standard care.
Therapy for the cohort is defined by the usual treatment strategy applied by rheumatologists for the treatment of oligo-and polyarticular PsA. The initial therapy (step 1) in this arm is methotrexate mono-therapy (starting 15mg/week rising escalated to 25mg/week in 6 weeks). In addition, all patients will be administered triamcinolone 80mg or depomedrol 120mg intramuscular (IM). In cases of non-response, sulfasalazine twice daily 1000mg will be added to the methotrexate (step 2). In case of failure of these two DMARDs, treatment will be escalated by adding a biological DMARD. In this study is opted for a TNF blocker (step 3). When the combination of conventional DMARD and a first TNF blocker fails, the TNF blocker will be switched to a second TNF blocker (step 4). The choice of which TNF blocker to use is at the discretion of the treating rheumatologist. The dosing of TNF blockers will be the standard dose for PsA according to current guidelines in line with National reimbursement guidelines. In addition, folic acid 10mg/week will be subscribed in every step of the escalation scheme.

ARM 2: Secukinumab
All participants will be prescribed secukinumab 300 mg every 4 weeks, with a

loading scheme of the first 4 300 mg injections weekly, in combination with methotrexate 15mg/week. In addition, all patients will be administered triamcinolone 80 mg or depomedrol 120mg intramuscular (IM). (step 1). Secukinumab is not registered for the first line treatment of PsA patients and is not in accordance with national reimbursement guidelines and therefore provided by Novartis. In case the first step fails (secukinumab 300mg + methotrexate 15mg/week) treatment will be switched to a TNF blocker (step 2) and to a second TNF blocker if the first TNF blocker fails (step 3). The choice of which TNF blocker to use is at the discretion of the treating rheumatologist. The dosing of TNF blockers will be the standard dose for PsA according to current guidelines in line with national reimbursement guidelines. When a second TNF blocker fails, this drug will be switched to apremilast 30mg twice daily (step 4). Apremilast therapy is in line with national reimbursement guidelines. In addition, folic acid 10mg/week will be subscribed in every step of the escalation scheme.

Study burden and risks

In our opinion, the implementation of this study is justified when we take into account the number of study visits for the patient/burden of filling out the questionnaires in relation to the knowlegde we are expecting to gain from this study.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. A new diagnosis of PsA as per CASPAR criteria at least 3 months.
2. A minimum of two swollen joints.
3. Patients must be able to understand and communicate with the Investigator and comply with the requirements of the study and must give a written, signed and dated informed consent before any study assessment is performed.
4. Male or female patients between 18 and 80 years of age.
5. Female participants of child bearing potential and male participants whose partner is of child bearing potential must be willing to ensure that they or their partner use effective contraception during the trial and for 3 months thereafter as in standard practice.

Exclusion criteria

1. Evidence of ongoing infectious or malignant process obtained within 3 months prior to screening and evaluated by a qualified health care professional.
2. Current or previous treatment of arthritis with DMARDs (including methotrexate, leflunomide or sulfasalazine) or biologics (including TNF, IL12/23 or IL17 inhibitor therapies)
3. Pregnant or nursing (lactating) women, in which pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive human chorionic gonadotropin (hCG) laboratory test.
4. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of study drug.
5. Underlying metabolic, hematologic, renal, hepatic, pulmonary, neurologic, endocrine, cardiac, infectious or gastrointestinal conditions which in the opinion of the Investigator immunocompromises the patient and/or places the patient at unacceptable risk for participation in an immunomodulatory therapy.
6. Significant medical problems or diseases, including but not limited to the following: uncontrolled hypertension (>= 160/95 mmHg), congestive heart failure (New York Heart Association status of class III or IV), and uncontrolled diabetes.

7. History of clinically significant liver disease or liver injury as indicated by abnormal liver function tests (LFT) such as aspartate aminotransferase/serum glutamic oxaloacetic transaminase (AST/SGOT), alanine aminotransferase/ serum glutamic pyruvic transaminase (ALT/SGPT), alkaline phosphatase, or serum bilirubin. The Investigator should be guided by the following criteria: Any single parameter may not exceed 2 x upper limit of normal (ULN). A single parameter elevated up to and including 2 x ULN should be re-checked once more as soon as possible, and in all cases, at least prior to enrollment/randomization, to rule out laboratory error.
8. History of renal trauma, glomerulonephritis, or subjects with one kidney only, or a glomerular filtration rate (GFR) < 30 ml/min.
9. Active systemic infections during the last two weeks (exception: common cold) prior to randomization.
10. History of ongoing, chronic or recurrent infectious disease or evidence of tuberculosis infection as defined by either a positive PPD skin test or a positive QuantiFERON TB-Gold test untreated or insufficiently treated according to the national guideline.
11. Known infection with human immunodeficiency virus, hepatitis B or hepatitis C at screening or randomization.
12. History of lymphoproliferative disease or any known malignancy or history of malignancy of any organ system within the past 5 years (except for basal cell carcinoma or actinic keratoses that have been treated with no evidence of recurrence in the past 3 months, carcinoma in situ of the cervix or non-invasive malignant colon polyps that have been removed).
13. Current severe progressive or uncontrolled disease, which in the judgment of the clinical Investigator renders the patient unsuitable for the trial.
14. Inability or unwillingness to undergo repeated venipuncture (e.g. because of poor tolerability or lack of access to veins).
15. Any medical or psychiatric condition which, in the Investigator*s opinion, would preclude the participant from adhering to the protocol or completing the study per protocol.
16. History or evidence of ongoing alcohol or drug abuse, within the last 6 months before randomization
17. Corticosteroid use within 8 weeks prior to randomization if used intra-muscular or oral and within 4 weeks prior if used intra-articular.

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:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	23-12-2019
Enrollment:	120
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:	08-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	07-08-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	21-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2018-004724-11-NL
CCMO	NL68512.078.18