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Comparing the effectiveness of morning and evening dosing of tofacitinib in inflammatory arthritis

Submission date
25/11/2021

Recruitment status
No longer recruiting

Registration date
22/12/2021

Overall study status
Ongoing

Last Edited
16/01/2025

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims:
Circadian rhythms are physical, mental, and behavioral changes that follow a 24-hour cycle. Disruption of the circadian rhythm may lead to immune system dysregulation. In line with this, various inflammatory arthritis symptoms show a distinctive daily pattern, including pain and joint stiffness. However, in daily practice we often do not take advantage of these circadian rhythms, especially not with regard to treatment. The aim of this study is to compare the effectiveness of tofacitinib morning versus evening dosing in rheumatoid arthritis and psoriatic arthritis patients.

Who can participate?
Patients aged 18 years or older with rheumatoid arthritis or psoriatic arthritis with active disease

What does the study involve?
Patients are randomly allocated to morning or evening dosing of tofacitinib for 3 months, which is followed by switching to the other treatment schedule for the next 3 months. Patients will be assessed at the start of the study and after 1, 3 and 6 months of treatment. At each visit patients will fill out online questionnaires and are seen by the research nurse. Additional blood and faecal samples will be taken at the start of the study and after 1 month (only blood), 3 and 6 months. Finally, patients will wear an actigraph (like a wristwatch) on their wrist two times for 2 weeks at home. The actigraph will be picked up by the patient in the hospital 2 weeks before the visit.

What are the possible benefits and risks of participating?
If successful, this study will show the best dosing time of tofacitinib and could be a step towards the use of this treatment on a regular basis in daily practice. It may also help better address well-known problems such as morning stiffness and fatigue, which often persist after reaching low disease activity.
Tofacitinib is approved and used according to the label so evening dosing of tofacitinib should not lead to any greater risks compared to morning dosing (routine care).

Where is the study run from?
Erasmus Medical Center, Rotterdam (The Netherlands)

When is the study starting and how long is it expected to run for?
January 2021 to October 2026

Who is funding the study?
Pfizer B.V. (USA)

Who is the main contact?
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Scientific

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Additional identifiers

EudraCT/CTIS number
2021-004131-84

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ChronIA001

Study information

Scientific Title
Chronotherapy in Inflammatory Arthritis: a randomized controlled trial comparing the effectiveness of morning and evening dosing of tofacitinib extended-release

Acronym
ChronIA

Study objectives
Evening dosing of tofacitinib XR will lead to a lower (self-reported) disease activity and improve sleep quality, morning stiffness and pain compared to morning dosing, because it is better synced with the circadian rhythm of inflammatory cytokines.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/02/2022, Medisch Ethische Toetsings Commissie (METC) Erasmus Medical Center (Postbus 2040, 3000 CA Rotterdam, the Netherlands; +31 107033625; metc@erasmusmc.nl), ref: NL78735.078.21

Study design
Open-label randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Inflammatory arthritis (rheumatoid arthritis and psoriatic arthritis)

Interventions

Patients will be randomized using minimization randomization stratified for diagnosis and co-medication. Patients are randomized into morning or evening dosing of tofacitinib XR (11 mg q. d.) for 3 months, which is followed by switching to the alternate regimen for the next 3 months.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Tofacitinib extended release

Primary outcome measure
Disease activity measured with the Routine Assessment of Patient Index Data 3 (RAPID3) at 3 months

Secondary outcome measures
Current secondary outcome measures as of 21/11/2023:
1. (Self-reported) disease activity (states) measured using Disease Activity Score (DAS) & Disease activity in PSoriatic Arthritis (DAPSA) at 3 and 6 months
2. Sleep measured using a sleep scale from the medical outcomes study (MOSS-ss) at 3 and 6 months
3. Morning stiffness (severity and duration) measured using a 10-point Likert scale at 3 and 6 months
4. Pain measured using a visual analogue scale (VAS) and the generalized pain questionnaire (GPQ) at 3 and 6 months
5. Fatigue measured using a visual analogue scale (VAS) and the Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) at 3 and 6 months
6. General health measured using a visual analogue scale (VAS) at 3 and 6 months
7. Functional ability measured using the health assessment questionnaire disability index (HAQ-DI) at 3 and 6 months
8. Quality of life measured using EuroQoL (EQ-5D-5L) at 3 and 6 months
9. Worker productivity measured using the Work Productivity and Activity Impairment (WPAI) at 3 and 6 months
10. Treatment satisfaction measured using a visual analogue scale (VAS) at 3 and 6 months
11. Compliance measured using the Medication Adherence Report Scale (MARS-5) at 3 and 6 months

Previous secondary outcome measures:
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3. Morning stiffness (severity and duration) measured using a 10-point Likert scale at 3 and 6 months
4. Pain measured using a visual analogue scale (VAS) at 3 and 6 months
5. Fatigue measured using a visual analogue scale (VAS) and the Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) at 3 and 6 months
6. General health measured using a visual analogue scale (VAS) at 3 and 6 months

7. Functional ability measured using the health assessment questionnaire disability index (HAQ-DI) at 3 and 6 months
8. Quality of life measured using EuroQoL (EQ-5D-5L) at 3 and 6 months
9. Worker productivity measured using the Work Productivity and Activity Impairment (WPAI) at 3 and 6 months
10. Treatment satisfaction measured using a visual analogue scale (VAS) at 3 and 6 months
11. Compliance measured using the Medication Adherence Report Scale (MARS-5) at 3 and 6 months

Overall study start date
01/01/2021

Completion date
31/10/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/11/2023:
1. Age ≥18 years
2. Diagnosed with rheumatoid arthritis (RA) or psoriatic arthritis (PsA), according to respectively the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 criteria for RA and ClASsification for Psoriatic ARthritis (CASPAR) criteria
3. Active disease, defined as a Disease Activity Score (DAS) >2.4 or Disease Activity in PSoriatic Arthritis (DAPSA) score >14

Previous inclusion criteria:
1. Age ≥18 years
2. Diagnosed with rheumatoid arthritis (RA) or psoriatic arthritis (PsA), according to respectively the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 criteria for RA and ClASsification for Psoriatic ARthritis (CASPAR) criteria
3. Active disease, defined as a Disease Activity Score (DAS) >2.4 or Disease Activity in PSoriatic Arthritis (DAPSA) score >14
4. Biological disease-modifying antirheumatic drug (bDMARD) usage <3

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
84

Key exclusion criteria
1. Current or previous treatment with a targeted synthetic (ts)DMARD
2. Prednisone (or equivalent) at a dose of >7.5 mg
3. (Relative) contraindications for the study medication
4. Work in shifts
5. Not being able to understand, speak and write in Dutch

Date of first enrolment
01/03/2022

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
Netherlands

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Study participating centre
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Hospital/treatment centre

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https://www.erasmusmc.nl/en/research/departments/rheumatology

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. Plans for sharing additional documents are currently unknown.

Intention to publish date
31/12/2027

Individual participant data (IPD) sharing plan
The current data-sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date