COntinuation Versus Interruption of Immunomodulating Drugs in case of an Infectious disease in IMID patients (COVID I2 study), with special attention for COVID 19: a pragmatic, explorative randomized controlled trial

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

Summary

ID

NL-OMON22848

Source
Nationaal Trial Register

Brief title
COVID I2

Condition

- Autoimmune disorders

Health condition

Rheumatoid arthritis

Psoriatic arthritis

Axial spondyloarthritis

Immune mediated inflammatory diseases

Inflammatory rheumatic diseases

Research involving
Human

Sponsors and support

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

Intervention

- Other intervention

Explanation

Outcome measures

Primary outcome

Proportion of participants with a serious infection, i.e. grade 3 or higher (according to the Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0).

Secondary outcome

- Patient characteristics: age, gender, weight, length, smoking habits, education, paid work characteristics, health care worker yes/no, having received influenza vaccination yes/no, other vaccinations, marital status, co-morbidities (cardiovascular disease, hypertension, diabetes) - Disease characteristics: diagnosis/diagnoses, year of diagnosis, history of severe infection - Treatment characteristics: (number of) previously used IA drugs, current medication, number of consultations with care providers - Medication use over time: use of IA medication (including prednisone), NSAIDs and ACE inhibitors during study period - Adverse events: occurrence of other (serious) adverse events during the study period. - Behavioural and environmental characteristics: compliance to Dutch COVID regulations (work at home if possible, social distancing) yes/no, positive or suspected COVID-infection within household yes/no. - Incidence of clinical infection (later validated and expanded using chart review, see definition in table 2), independent of location, type of infection, or severity. - Infection characteristics: severity (Grade), infection duration (days until resolution), recurrence of infection, antibiotics use, hospital admission (+duration), surgery, IC-admission (+ duration, use of vasoconstrictive medicine), death - IMID-related flares, defined by the patient (‘are you currently experiencing, or did you experience a flare-up of your disease’ yes/no) - Direct

medical costs (medication, consultations with general practitioner/specialists, hospitalization, intensive care admission, surgery)

Study description

Background summary

Immunomodulatory agents (IA) are widely used (>200,000 patients in the Netherlands) for the treatment of patients with immune-mediated inflammatory diseases (IMIDs) including rheumatoid arthritis, psoriatic arthritis, axial spondylarthritis, psoriasis and inflammatory bowel disease, and they are in general associated with a modestly increased risk of infection. However, it is not clear what risk factors for infection are, and whether it is wise to temporary interrupt IA treatment during an infection. Recently, the COVID-19 pandemic has dramatically increased the urgency to provide answers to these questions, especially since, surprisingly, some IA seem to be effective treatment against COVID-19. Therefore, the objectives of this study are to: 1) To assess the effect of continuation of IA treatment in IMID patients during an infection compared to temporary interruption of the IA treatment with regard to serious infection, and 2) to study the incidence and risk factors for infection in IMID patients using IA, with special attention for COVID-19. This study is a two arm, open-label pragmatic, explorative randomized controlled strategy study, among IMID patients using IA in the Netherlands. Adult patients with rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, psoriasis and inflammatory bowel disease using IA (except monotherapy rituximab or glucocorticoids) in any dose without a current infection will be included and randomized into either the intervention or control group. The intervention consists of continued IA treatment and the control condition is interruption of IA treatment until the infection is resolved, all in addition to standard of care. Main study parameters/endpoints: The primary outcome is serious infection (resulting in hospitalization, intravenous antibiotics, admission to the intensive care or death)

Study objective

As this is an explorative design, no formal hypothesis is made. However, our sample size is based on a difference of 2.5% or more in cumulative incidence of serious infections when continuing IA, hypothesizing that patients who continue their IA in case of an infection experience less severe infections compared to patient who temporarily interrupt IA.

Study design

Patients will be followed for 12 months, receiving questionnaires at baseline and one each following month. If a patient experiences an infection at t = 12 months, he/she will be followed until the infection has passed. In addition, data will be collected in case of an infection.

Intervention
Continuation of immunomodulatory medication during an infection

Contacts

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Eligibility criteria

Age
Adolescents (16-17 years)
Adolescents (16-17 years)
Adults (18-64 years)
Adults (18-64 years)
Elderly (65 years and older)
Elderly (65 years and older)

Inclusion criteria

- Clinical diagnosis of at least one of the following IMIDs: Rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA), psoriasis (PsO) or inflammatory bowel disease (IBD) (i.e. Crohns disease (CD) or ulcerative colitis (UC). - Age ≥ 16 years - Using one or more of the following immunomodulating agents (IA) from table 1 in any dose. Monotherapy rituximab and glucocorticoids are exempts because rituximab cannot be stopped due to long half-life time and post pharmacokinetic effects on b-cell depletion, and glucocorticoids because stopping is associated with secondary hypocortisolism. - Not experiencing any clinical infection at time of inclusion (based on check in electronic health record and as reported by patient at inclusion). - Ability to read and communicate well in Dutch

Exclusion criteria

- Use of the following immunomodulating agents in monotherapy and through intravenous

administration: rituximab, tocilizumab or abatacept. This because the contrast between stopping and continuation is expected to be low, as the treatment intervals are high, and intravenous medication is not easily provided in case of hospital admission. - Use of glucocorticoids (GC) in monotherapy, because stopping of GC is not feasible due to risk of GC use induced hypocortisolism - Not willing to be randomized to either intervention or control condition. - Not being able to be followed for 12 months, because of planned relocation or short life expectancy.

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:	Recruitment stopped
Start date (anticipated):	08-10-2020
Enrollment:	2200
Type:	Actual

IPD sharing statement

Plan to share IPD: Yes

Plan description
Individual de-identified participant data will be made available to researchers who provide a methodologically sound proposal to achieve aims in the approved proposal or for individual participant data meta-analyses. Data requestors will need to sign a data access agreement.

Ethics review

Approved WMO Date:	20-07-2020
Application type:	First submission
Review commission:	METC Oost-Nederland

Study registrations

Followed up by the following (possibly more current) registration

ID: 54899
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8922
CCMO	NL73479.091.20
OMON	NL-OMON54899

Study results