Dose reduction of the new generation biologicals (IL17 and IL23 inhibitors) in psoriasis: A pragmatic, multicentre, randomized, controlled, non-inferiority study - BeNeBio study

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22341

Source
NTR

Brief title
BeNeBio

Health condition

Psoriasis

Sponsors and support

Primary sponsor: Radboudumc
Source(s) of monetary or material Support: ZonMW, KCE

Intervention

Outcome measures

Primary outcome

Non-inferiority of the incidence proportion of persistent flares (PASI > 5 for ≥ 3 months) in the intervention group.

Secondary outcome

• Whether participants will have successful DR after 12 and 18 months, defined as using a lower dose than the normal dose and PASI ≤ 5.
• Psoriasis disease activity, measured with the Psoriasis Area and Severity Index (PASI) at each 3-monthly study visit.
• Dermatology-related quality of life as measured with the Dermatology Life Quality Index (DLQI) at each 3-montly study visit.
• Whether participants will have short disease flares throughout the study period (18 months), defined as a PASI > 5 at one time point.
• Whether other anti-psoriatic medication will be initiated in participants during the study period (18 months).
• Whether participants will have serious adverse events (SAE) and adverse events of special interest (AEoSI) during the study period. AEoSI include, but are not limited to, infections, malignancies, and joint complaints or new-onset psoriatic arthritis.
• Drug trough levels of each included drug, measured in blood serum samples which will be collected from participants at each 3-montly time point.
• Anti-drug antibody levels of each included drug, measured in blood serum samples which will be collected from participants at each 3-montly time point.
• Utilities, derived from EuroQoL 5 Dimensions (EQ-5D-5L) questionnaires, which will be measured at each 3-montly time point. Utility scores will be used to calculate quality adjusted life years (QALYs) which are used to determine cost-effectiveness of DR.
• Health status of participants, assessed by using the Short Form 36 (SF-36) version 2 questionnaire at every 3-monthly time point.
• Volumes of care, as measured with the iMTA Medical Consumption Questionnaire (MCQ) at each 3-monthly time point.
• Loss of productivity and presenteeism of participants, as measured with the iMTA Productivity Cost Questionnaire (PCQ) at each 3-monthly time point.

Study description

Background summary

Rationale: Biologics are very effective treatments for psoriasis. Research indicated that the dose of TNFα-blocking biologics can be reduced in a proportion of patients. Safety profiles can improve and costs can be reduced if the reduction of the dose is successful. Recently, the newest generation of biologics entered the market: interleukin (IL) 17 and IL23 inhibitors. These biologics are increasingly prescribed. It is not yet known whether dose reduction of these agents is possible, and to what extent they can be reduced. The new agents have different mechanisms of action and safety profiles compared to TNFα-blockers. The timely investigation of the possibilities for dose reduction of new biologics is therefore important.

Objectives: The primary goal is to investigate whether controlled dose reduction of IL17 or IL23 inhibiting biologics is not inferior compared to usual care. This is measured by comparing the proportion of long-term disease flares between the two groups (dose reduction group versus usual care group). Secondary goals are: determining the proportion of patients with successful dose reduction, clinical effectiveness measured with the Psoriasis Area and Severity score (PASI) score, Dermatology Life Quality Index (DLQI) scores, predictors for successful dose reduction, safety, and cost-effectiveness of dose reduction. Pharmacokinetic (PK) analysis will be performed for modeling.
Study design: a multicenter, practice-oriented, pragmatic, randomized, controlled, non-inferiority study.
Study population: Patients treated with the newest generation of biologics (IL17 or IL23 inhibitors), with long-term stable low disease activity at a normal dose. A total of 244 patients are randomized (2:1) to dose reduction or continuation of usual care.
Intervention: Dose reduction by interval prolongation in 2 steps to a maximum decrease of 50% of the original dose when disease activity (PASI) and quality of life index (DLQI) remain low.
Disease outcomes: Primary outcome is the cumulative incidence of persistent flares (PASI> 5 for ≥ 3 months). Secondary outcomes are the percentage of successful dose reductions, the course of disease activity (PASI), incidence of short disease flares (PASI> 5 once), course of disease-related quality of life (DLQI), predictors for successful dose reduction, side effects, antibody formation and trough levels of biologics (PK), health-status (SF-36), quality-adjusted life-years (EQ-5D-5L), volumes of care (iMTA Medical Consumption Questionnaire), loss of productivity and presenteeism (Productivity Cost Questionnaire).
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: There is a risk for disease exacerbation due to dose tapering. This risk will be kept as low as possible by strictly monitoring the patients and change therapy in case of increasing PASI scores and/or DLQI index to an unacceptable level. The burden of this study regarding study measurements is expected to be minimal: (non-invasive) disease severity measurements will be performed, like PASI scores that are already standard of care in some of the centres (5 minutes extra time). Patients will be asked to fill in 4 questionnaires on quality of life and costs every 3 months during the study (approx. 20 minutes duration). Every 3 months, one extra vial of blood will be asked from the patients, most of the time this will be done at moments when blood is already drawn for usual care. There is direct individual benefit only in those patients that can be reduced in dose. On group level, the safety profile of these new drugs is expected to improve, and costs are expected to decrease by at least 30% with the proposed strategy in patients with stable disease.

Study objective

Controlled dose reduction of IL17 or IL23 inhibiting biologics is not inferior compared to usual care.

Study design

18 months

Intervention

Intervention: dose reduction of IL17 and IL23 inhibitors (Secukinumab, Ixekizumab, Brodalumab, Guselkumab, Risankizumab, Tildrakizumab)
Control: normal (registered) dose

Contacts

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Eligibility criteria

Inclusion criteria

• Plaque psoriasis (primarily)
• Treatment for at least 6 months with IL23 or IL17 inhibitor in a normal dose (dose advised by the label)
• PASI≤ 5 at inclusion and in previous 6 months (if no PASI scores are available, it should be clear from the patient record that psoriasis was clear/almost clear in previous 6 months).
• DLQI ≤ 5 at inclusion

Exclusion criteria

• Another indication than plaque psoriasis as the main indication for biologic use (e.g. patient receives biologic for rheumatoid arthritis as the main indication).
• Concomitant use of systemic immunosuppressants other than methotrexate or acitretin (e.g. prednisone, cyclosporine etc).
• Severe comorbidities with short life-expectancy (e.g. metastasized tumor).
• Presumed inability to follow the study protocol.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	20-08-2020
Enrollment:	244
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	20-03-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 52624
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8470
CCMO	NL71920.091.19
OMON	NL-OMON52624

Study results