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

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON52624

Source
ToetsingOnline

Brief title
Dose reduction of IL17 and IL23 inhibitors for psoriasis

Condition

- Epidermal and dermal conditions

Synonym
psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw;KCE (Belgie)

Intervention

Keyword: biologic, dose reduction, IL23, psoriasis

Outcome measures

Primary outcome

Primary outcome is the cumulative incidence of persistent flares (PASI> 5 for >= 3 months).

Secondary outcome

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).

Study description

Background summary

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.

Study objective

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 burden and risks

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. 10 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.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

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

Exclusion criteria

• Another indication than plaque psoriasis as the main indication for biologic use (e.g. 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 tumour).
• Presumed inability to follow the study protocol.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-08-2020
Enrollment:	142
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cosentyx
Generic name:	Secukinumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Ilumetri
Generic name:	Tildrakizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Kyntheum
Generic name:	Brodalumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Skyrizi

Generic name:	Risankizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taltz
Generic name:	Ixekizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-02-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-03-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-12-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-05-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-05-2022

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 22341
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2019-004230-42-NL
ClinicalTrials.gov	NCT04340076
CCMO	NL71920.091.19