Effect of inhaled corticosteroid tapering in obese T2-low asthma patients on asthma control and quality of life: an investigator-initiated, multicenter, non-inferiority, open label crossover trial with open label extension

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Primary Objective To demonstrate that ICS can be safely withdrawn in T2-low asthma patients with obesity in secondary care (i.e. without loss of asthma control).Secondary Objectives1. To determine predictive factors for successful ICS withdrawal.2....

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON55120

Source
ToetsingOnline

Brief title
Steroid Tapering in Obese Patients with type 2 low asthma (STOP)

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Bronchial disorders (excl neoplasms)

Synonym
(T2-low/obese) asthma

Research involving
Human

Sponsors and support

Primary sponsor: Franciscus Ziekenhuis
Source(s) of monetary or material Support: BeterKeten

Intervention

Keyword: Asthma, ICS, Obesity, Tapering

Outcome measures

Primary outcome

Endpoint:

- Demonstrating sustained asthma control after ICS tapering

Definitions of sustained asthma control:

- No significant difference in ACQ score between ICS tapering and ICS continuation when corrected for the baseline value and with a non inferiority margin of 0.25 ACQ points (5%)

Secondary outcome

Anamnestic - History of relevant allergies

- Exacerbation frequency (mild/intermediatie/severe)

- Medication

- Smoking status and exposure to drugs/vapours/fumes/gases/other chemicals

- Social economic status

- Age at asthma diagnosis

- Co-morbidity (such as hypertension, OSAS, cardiovascular disease,

stroke, diabetes, kidney failure, gastro-intestinal reflux,

malignancy,

osteoporosis)

- Birth weight and respiratory history during childhood

- Adverse events

Questionnaires- ACQ

- AQLQ

- MRC

- FSS

Anthropometrics- BMI

- Waist circumference

- Blood pressure

- O2-saturation (standing/ supine)

Blood tests - Endocrine panel (including fasting glucose/insulin, lipid

spectrum,

liver function tests, haematologic parameters)

- Pulmonary panel (including eosinophils, total IgE)

- Transcriptomics, proteomics and metabolomics (e.g. *omics*)

Lung function - expiratory flow assessment

- FeNO

- eNose

Other - hair cortisol

Study description

Background summary

Asthma is a heterogeneous disease with increasing attention in the past years forits endotypes. Obesity-related asthma is an endotype with often a high burden of disease without noticeable T2 inflammation, the so-called T2 low endotype. However, their is no distinction between the treament of the differenct astma endotypes. ICS remains the cornerstone of asthma treatment in both primary and secondary care. Despite ICS treatment, the asthma control often remains poor in patients without T2 inflammation. Previous research from the FGV shows that weight loss does improve asthma control. Recent large-scale research from Erasmus MC shows that ICS can have adverse systemic effects and are associated with a higher BMI, larger waist circumference and other determinants of the metabolic syndrome. In addition, obese people use corticosteroids two to three times more often, which makes losing weight difficult. Nonetheless, both national- and international guidelines continue to adviese treatment with ICS for all astma patients. This is mainly due to lack of research in T2 low asthma. For example, to date, there are no good randomized studies demonstrating effectiveness of ICS in this specific group of T2-low asthma patients with obesity.

Study objective

Primary Objective
To demonstrate that ICS can be safely withdrawn in T2-low asthma patients with obesity in secondary care (i.e. without loss of asthma control).

Secondary Objectives
1. To determine predictive factors for successful ICS withdrawal.
2. To determine the effect of ICS withdrawal on determents of Metabolic Syndrome using physical examination (such as weight an blood pressure), blood- and hair tests (e.g. endocrine markers of metabolic syndrome and steroid levels)
3. To describe the effect of ICS on inflammatory biomarkers (e.g. proteomics and genomics) and physical parameters (e.g. lung function) in T2-low asthma.
4. To detect whether the T2-low status changes over time and during an exacerbation (i.e. detecting T2-hidden or false negative patients)
5. To further complement T2-phenotyping using exhaled molecular compounds

analyses (i.e. electronic nose or eNose) which gives inside in potential early biomarkers for low steroid efficacy.

Study design

An investigator-initiated multicenter non-inferiority open label randomized crossover study with open-label extension.

Intervention

- inclusion and randomisation into arm A and arm B

Run in:
- Fluticason 1000mcg per day plus Fenoterol/*ipratropium as needed for 4 weeks
- In case of progressive dyspneu, but no exacerbation: IOS/FeNO/Spiro and restart of LABA, after 2 weeks IOS/FeNO/Spiro/blood tests and eindpoint reached: end of trial

Arm A:
- 14 weeks fluticason 1000mcg/day

Arm B:
- 2 weeks fluticason 500mcg/day
- 2 weeks fluticason 250mcg/day
- 10 weeks no ICS

----- CROSSOVER -----

Arm A:
- 2 weeks fluticason 500mcg/day
- 2 weeks fluticason 250mcg/day
- 10 weeks no ICS

Arm B:
- 14 weeks fluticason 1000mcg/day

----- START EXTENSION-----

No study arms. Patients with sustained asthma control after ICS tapering may continue in a controlled extension study to study long term benefits of being ICS naïve. (Metabolic and endocrine parameters.)

Geen studie armen. Patiënten die succesvol hebben afgebouwd kunnen in een gecontroleerde setting 2 jaar meedoen aan de extensie studie. (Dit geeft informatie over zowel de lange termijn astma controle, alsook lange termijn voordelen van het stoppen met ICS op metabole en endocriene determinanten.)

Study burden and risks

The study requires the patients to visit the outpatient more often than usual (after inclusion 4 visits in 9 months). Additionally, patients wil lbe asked to complete a short questionnaire weekly, using an online application. In this application, patients will report the frequency of Fenoterol/*ipratropium use (escape medication). The patients will be instructed to contact the local investigator in case of worsening of asthma symptoms. In case of a significant increase of the ACQ (>= 0.5 points for >= 4 days) or in case of frequent use of escape medication (>6 inhalations of Fenoterol/*ipratropium per day), a consult by telephone will be scheduled. When the investigator suspects an exacerbation, the patient will be asked to visit the hospital, where the patient will receive usual care. In case of a second intermediate/severe exacerbation, the patient van no longer participate in the study and its extension.

During the visits at the outpatient clinic, some tests will be performed, only the vena puncture is (minimally) invasive.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- T2 low asthma (see protocol for definition)
- stable asthma (no exacerbation in past 3 months)
- BMI >= 25 kg/m2

Exclusion criteria

- Systematic use of oral, nasal or topical corticosteroids
- Use of immune suppressive drugs
- Other relevant disease, such as COPD or malignancy (see protocol for detailed list)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2021
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Berodual 50/20
Generic name:	Fenoterol/ipratropium 50/20
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Fluticasone aerosol 250mcg
Generic name:	Budesonide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-12-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-12-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-08-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-01-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

(Nieuwegein)

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: 23421
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTRNL73155.100.20-NL
CCMO	NL73155.100.20
OMON	NL-OMON23421