DUAL HOMING MECHANISMS OF EOSINOPHILS TO THE SPUTUM; ONLY ONE OF WHICH IS SENSITIVE FOR MEPOLIZUMAB

Published: 14-02-2017
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Objective: The objective of the study is establish the half-life of eosinophils in blood and sputum and determination of the effect of Nucala® hereon.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON45761

Source
ToetsingOnline

Brief title
FOOTSTEP

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma, shortness of breath

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: GlaxoSmithKline,Investigator sponsored

studies programma van GlaxoSmithKline (GSK)

Intervention

Keyword: asthma, eosinophil, kinetics, mepolizumab

Outcome measures

Primary outcome

Main study parameters/endpoints: the main study parameter is enrichment of 2H-DNA in the DNA of eosinophils obtained at different time points after labelling. The patients will be asked to drink 2H-glucose (1 g/kg) during 6 hrs at time -5 days before the start of the treatment. After 5 days labelled eosinophils will leave the bone marrow and the pulse of 2H-DNA can be followed in blood and sputum. The kinetics of the pulse relates with the half-life of the cells

Secondary outcome

The secundary parameters are:

1. Th17/Th2 cytokine profile in peripheral blood. Data will be determined by multiplex technology (Luminex)

2. Profile of eosinophil degranulation products in sputum samples.

Study description

Background summary

Eosinophil asthma, particularly the steroid unresponsive form, benefits from treatment with a monoclonal antibody (Mepolizumab/Nucala®) directed against IL-5 (terminal differentiation factor of eosinophils) The underlying mechanism is unclear as treatment with Nucala® needs > 6 months in order to establish a

significant clinical effect, whereas the effect on eosinophils in blood and bone marrow is evident after 1-2 weeks.

Study objective

Objective: The objective of the study is establish the half-life of eosinophils in blood and sputum and determination of the effect of Nucala® hereon.

Study design

Study design: the study is double-blind placebo controlled intervention study.

Intervention

Intervention (if applicable): the intervention is treatment with Nucala® (100 mg subcutaneously every 4 weeks/4 doses) or with placebo (saline, every 4 weeks/4 doses).

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: the burden of the study is relatively high as the patients are asked to come for two days to the UMCU for the labelling days with 2H-glucose en for 10 visits for donation of blood (10 min) and 3 times donation of induced sputum 30 min. The risks of the study are minimal: no adverse effects has been linked to the treatment with Nucala® other than mild and reversible symptoms such as common cold, headache, nasal congestion, back pain and pyrexia. The labelling with 2H-glucose is safe as there has been no documented negative effects at the dose that is used in the study. Both venapunction and production of induced sputum are considered safe and cause only mild discomfort. Induced sputum might induce a mild shortage of breath that is easily treated with beta-2 agonists (bronchus dilators). The eosinophilic asthma patients are chosen as they have sufficient numbers of eosinophils in blood and sputum and Nucala® is registered for this patient group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Age > 18 and younger than 70 years
* Diagnosis of eosinophil asthma despite use of corticosteroids
* Suitable for sputum induction
* >2.5% sputum eosinophils OR blood eosinophils > 0.25x10^9/L

Exclusion criteria

* Any acute or chronic infection (eg. HIV, Hepatitis, STDs, pneumonia, influenza etc.)
* Insulin dependent diabetes
* Smoking at present or in the last 12 months and/or a past history of more than 10 pack years
* Proven allergic bronchopulmonary aspergillosis
* Auto-immune diseases
* Use of immune modulating medication (such as NSAID's, monoclonal antibodies, purine antagonistis etc.) excluding:
o Steroids used to treat asthma
* exuberant alcohol consumption (for males > 36 glasses per week, for females >24 glasses per week)
* Drug use

* Active cancer or a cancer diagnosed < 5 years ago.
* Unstable disease despite high dose of systemic steroids (20 mg prednisolon or more)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-06-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nucala
Generic name:	Mepolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	14-02-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date:	26-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-01-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-002014-52-NL
CCMO	NL57535.041.16