Drivers of Eosinophilic COPD Exacerbations

Published: 11-03-2021
Last updated: 08-04-2024

Main objective: investigate gene expression differences in nasal epithelium and sputum between eosinophilic COPD exacerbations and other subtypes. Secondary objectives: 1. Investigate differences in microbiome composition and immunophenotyping...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational invasive

Summary

ID

NL-OMON54085

Source
ToetsingOnline

Brief title
DICE

Condition

- Bronchial disorders (excl neoplasms)

Synonym
chronic obstructive pulmonary disease, emphysema and chronic bronchitis.

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: - ,GlaxoSmithKline

Intervention

Keyword: COPD, Eosinophilic, Exacerbation

Outcome measures

Primary outcome

Gene expression differences in sputum and nasal epithelium between eosinophilic COPD exacerbations and other subtypes.

Secondary outcome

1. Microbiome composition and immunophenotyping profiles of the different subtypes, i) eosinophilic, ii) viral, iii) bacterial, iv) pauci-inflammatory.

2. Course and duration of symptoms, measured by changes in peak flow and CAT scores.

3. RNA sequencing in nasal epithelium and sputum, and immunophenotyping in blood.

4. Differences in the sputum and nasal epithelial microbiome between COPD exacerbation subtypes, both during stable state and exacerbations.

5. Per subtype: course and duration of symptoms (CAT questionnaire), and lung function recovery after exacerbation, duration of hospital admission, risk of 2nd exacerbation during the follow-up.

Study description

Background summary

Acute COPD exacerbations are heterogeneous of nature and can be grouped into specific biologic clusters. Moreover, there are unique microbial compositions within these clusters of acute exacerbations of COPD. This suggests that each COPD patient carries a unique microbiome composition and that this composition

drives an immunological response during an exacerbation through cross-talk with the host. Meta-transcriptomic analyses of respiratory samples can simultaneously assay microbial and host genomes to identify microbial transcriptional changes and host gene expression responses. However, the exact immunological response orchestrating the cross-talk between microbiome and host response during an AECOPD remains elusive.

Study objective

Main objective: investigate gene expression differences in nasal epithelium and sputum between eosinophilic COPD exacerbations and other subtypes.
Secondary objectives:
1. Investigate differences in microbiome composition and immunophenotyping profiles in peripheral blood per subtype.
2. Assess for clinical differences between all COPD exacerbation subtypes.
3. Assess if and how baseline meta-transcriptomics either in nasal epithelium or sputum and blood immunophenotyping can be utilized to predict COPD exacerbation subtype.
4. Determine if the microbiome in sputum and nasal epithelial material are comparable.
5. Determine if different subtypes of COPD exacerbations respond differently to standard treatment with oral prednisolone (40 mg daily) with or without antibiotics.

Study design

In this prospective observational study, data and samples will be collected from 100 COPD patients at time of hospitalization for a severe COPD exacerbation, and in stable state, 6-8 weeks after onset of the exacerbation. If a second exacerbation occurs, more data and samples will be collected. Moreover, subjects will be followed-up for the duration of one year after inclusion to register symptoms by means of a telephone assessment. This is a multicentre study.

Study burden and risks

There are several burdens for participants in this study. Participants will have to visit the study hospital, fill in the questionnaires and take peak flow measurements several times. Extra blood will be drawn (3x56.5ml) and nasal brushes will be taken. When necessary, a subject will be asked to undergo a sputum induction. These procedures cause several risks. Venipuncture may cause a local hematoma, acquiring nasal brushes may cause a nose bleed, sputum induction may lead to transient bronchospasm and dyspnea.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- COPD patient admitted to the hospital for an acute exacerbation - A physician diagnosed COPD according to the GOLD 2017 guidelines - Age >40 years - Smoker or ex-smoker, >10 pack years of smoking

Exclusion criteria

- Current asthma or prior physician diagnosis of asthma without a symptom-free interval of at least 10 years before the age of 40 - Use of systemic corticosteroids >-4 days prior to hospital admission - Necessity (upon hospitalization) for non-invasive ventilation or ICU admission - Pneumonia at hospital admission, defined by the clincal presentation and the presence of a

lobar consolidation on radiographical imaging - Any other clinically relevant lung disease deemed to interfere with the concept of the study design - Pregnancy and lactation.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-07-2021
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	11-03-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Not approved

Date:	11-08-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	15-09-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	11-07-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL75151.042.20