3TR - ABC (Asthma Biologics Cohort) study and AIR-Bio-OCT study
A part of the 3TR (Taxonomy, Treatment, Targets and Remission) Consortium for the identification of the molecular mechanisms of non-response to treatment, relapses, and remission in autoimmune, inflammatory, and allergic conditions

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The overall aim of the study is to improve personalized medicine for patients with severe asthma through the investigation of possible immunological mechanisms responsible for non-response or incomplete response to biological treatments.2.1 3TR -...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Observational invasive

Summary

ID

NL-OMON52133

Source
ToetsingOnline

Brief title
3TR- ABC Study and AIR-Bio-OCT study

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
"severe asthma", "uncontrolled asthma"

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: NWO,Astra Zeneca,Innovative Medicine Initiative;Astra Zeneca

Intervention

Keyword: biomarkers, non-response, response, severe asthma

Outcome measures

Primary outcome

3TR-ABC:

To determine super responders, clinical responders, and non-responders of the

real-life severe asthma cohort.

AIR Bio-OCT:

Establish minimal invasive prediction 'signatures' for Benralizumab response in

severe asthma by multilevel non-invasive exhaled breath -omics approach.

Secondary outcome

3TR-ABC:

To identify and describe differences in biomarker profiles between super

responders, clinical responders, and non-responders.

AIR Bio-OCT Study

Establish a change in extra cellular matrix (ECM) and airway smooth muscle mass

(ASM) by standard - PS-OCT and endobronchial biopsy analysis after 52 weeks of

Benralizumab treatment (15 patients).

Study description

Background summary

Severe asthma has a large impact on the quality of life of patients and their families. New biological treatments (eg. Mepolizumab, Benralizumab, Reslizumab, Dupilumab, Tezepelumab) are currently available to treat severe asthma patients. However, not all severe asthma patients respond equally to these treatments and we hypothesize that airway inflammation and remodeling are pivotal therein, including the reduction in airway smooth muscle (ASM) mass and extra-cellular matrix (ECM) alterations. Current gold standard techniques to assess changes in airway remodelling (e.g. high-resolution computed tomography (HR-CT) of the chest or endobronchial sampling) have their limitations. In this project we aim: 1) to unravel phenotypes and mechanisms responsible for insufficient treatment response of biologics, with the ultimate aim to reveal novel treatment targets in severe asthma patients and 2) to unravel Benralizumab specific phenotypes and the impact of Benralizumab on airway remodeling by the use of Optical Coherence Tomography (OCT) in severe asthma patients.

Study objective

The overall aim of the study is to improve personalized medicine for patients with severe asthma through the investigation of possible immunological mechanisms responsible for non-response or incomplete response to biological treatments.

2.1 3TR - ABC Study objectives

Primary Objective:
• To establish a real-life cohort of patients with severe asthma commenced on a biological treatment.to determine super responders, clinical responders, and non-responders
Secondary Objective(s):
• To identify and measure immunologic biomarkers at baseline related to super-response versus clinical response versus non-response to biological

treatment of severe asthma.
• To identify which pathways that are not suppressed by treatment in non-responders versus responders (clinical and super).
• To identify and describe differences in biomarker profiles between super responders, clinical responders, and non-responders at baseline visit.
• To describe differences in changes in biomarker profiles between super responders, clinical responders, and non-responders.
• To identify the impact of super-, clinical-, and non-response on long-term outcomes (3 years).
• To identify predictors of persistent response/loss of response to biologic treatments.

Exploratory Objective(s):
• To network and make cluster analyses of omics data in order to determine possible novel biomarker signatures and relate these to clinical response.
• To compare and cross-validate known biomarker profiles with those derived from previously published severe asthma studies.

2.2 AIR-BIO-OCT substudy objectives

Primary Objective:
• To identify and measure an eNose/ volatile organic compound (VOC)-multi-omics extensive severe asthma phenotyping strategy before treatment with Benralizumab to reveal add-on response characteristics to better predict treatment response.
• To identify and measure minimal invasive predicting *signature* of Benralizumab treatment response in severe eosinophilic asthma by extensive asthma pheno-endotyping using innovative minimal invasive exhaled breath technologies including eNose/VOCs and omics.

Secondary Objective(s)
• To measure airway remodeling (extra cellular matrix and airway smooth muscle) after treatment with Benralizumab
• Establish the reduction of extra cellular matrix (ECM) and airway smooth muscle (ASM) by standard - polarization sensitive (PS) - OCT and endobronchial biopsy analyses after 52 weeks of Benralizumab treatment
• To reveal the airway wall delivery and cellular targets of Benralizumab in vivo by immune-OCT.

Study design

Observational multicenter study, for which the analyses will be done in a European consortium. Patients will be extensively characterized at baseline and then followed for 3 years. Data analyses will be performed in an international research consortium.

Study burden and risks

The burden and risks associated with participation of the study is limited for all sample collection except for bronchoscopy sampling which is considered moderate. For this, we have extensive experience with bronchoscopies with sampling including biopsies and (PS-)OCT imaging in severe asthma patients in our previous studies including TASMA study. In the future, the results of this study could lead to improved treatment allocation and novel treatments for severe asthma patients

Contacts

Public
Amsterdam UMC

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Amsterdam UMC

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients with severe asthma:
Patients with the age of >=18 years diagnosed with severe asthma and eligible for biologic treatment (in the Netherlands the 3TR- ABC Study will include patients with severe asthma eligible for Anti-IgE, Anti-IL5(R), and Anti-IL4/IL13 treatment.).

Patients are defined as having severe asthma if:

* High dose treatment in the last year:
o High dose ICS (corresponding to minimum 1600 micrograms Budesonide per day) + either LABA, LTRA, or LAMA
or
o Fixed Prednisolone treatment (OCS) minimum 50% of the time.

* Other reasons for lack of control excluded (systematic investigation according to guidelines for investigation of severe asthma)
and
* Minimum 2 exacerbations in the last year or fixed Prednisolone treatment (OCS) minimum 50% of the time.
•Clinical decision to initiate Initiation initiate biologic therapy for severe asthma after meeting licensing, local and national guidelines (Dupilumab, Mepolizumab, Benralizumab, Tezepelumab, Omalizumab or Reslizumab)

Mild/moderate asthma controls:
Patients of >=18 years with mild/moderate controlled asthma and markers of T2 inflammation (see table 2), or patients with low T2 inflammation, who are not candidates for biologic treatments.

Healthy controls:
Participants of >=18 years without any history of respiratory symptoms or recent infections, and who do not use any medication related to airway diseases or are in treatment for any other diseases that may influence respiratory biomarkers considerably.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

Severe asthma patients will be excluded if:
* Unable to understand written information due to language barriers.
* Unable to give informed consent, i.e., patients who are incapable.
* Unable to complete study visits.
- Usage of mainetenance OCS (only for patients starting dupiluman, as

part of the Sanofi funded arm, not the overall 3TR)

Exclusion criteria specifically for the AIR-BIo-OCT substudy patiënts:
- Patients have been treated with biologics for severe asthma <3 months before the inclusion.
- OCS use >20 mg daily.
- BMI >35.
- Have smoked > 15 pack years defined as (number of cigarettes smoked per day/20) × number of years smoked .
- Reports a diagnosis of EGPA, ABPA or other respiratory condition that interferes with Benralizumab

Mild/moderate asthma participants will be excluded if:
* Unable to understand written information due to language barriers.
* Unable to give informed consent, i.e., patients who are incapable.
* Show signs of symptoms of uncontrolled asthma (ACQ score higher than 1.5, OCS use, history of exacerbations within the past year).

Healthy participants will be excluded if:
* Unable to understand written information due to language barriers.
* Unable to give informed consent, i.e., patients who are incapable.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-01-2023
Enrollment:	75
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	11-11-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL77983.018.22