A PROSPECTIVE, SINGLE ARM, LONGITUDINAL COHORT STUDY TO ASSESS BIOMARKERS IN REAL WORLD PATIENTS WITH SEVERE ASTHMA

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Upper respiratory tract disorders (excl infections)
Study type	Observational invasive

Summary

ID

NL-OMON43783

Source
ToetsingOnline

Brief title
MB29599
Arietta

Condition

- Upper respiratory tract disorders (excl infections)

Synonym
chronic airwayinflammation, severe asthma

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: farmaceutische industrie F. Hoffmann la Roche Inc

Intervention

Keyword: biomarker, periostin, severe asthma

Outcome measures

Primary outcome

The outcome measures for this study are:

· Asthma exacerbation defined as:

- For patients who are not on maintenance oral corticosteroid therapy: new or increased asthma symptoms (including wheeze, cough, dyspnoea, chest tightness, and/or nocturnal awakening due to these symptoms) that lead to treatment with systemic corticosteroids or to hospitalization. Treatment with systemic corticosteroids is defined as treatment with oral, intravenous (IV), or intramuscular (IM) corticosteroids for * 3 days or an emergency department visit with at least one dose of IV or IM corticosteroids.

- For patients who are on maintenance oral corticosteroid therapy: new or increased asthma symptoms (including wheeze, cough, dyspnoea, chest tightness, and/or nocturnal awakening due to these symptoms) that lead to intensified treatment with systemic corticosteroids, defined as * 30 mg or 0.5 mg/kg for * 3 consecutive days, or to hospitalization.

- Note: hospitalization and systemic corticosteroid treatment criteria must be verified in medical records from the treating institution.

Additional details are provided in Appendix 2.

· Pre-bronchodilator FEV1

· Time to first asthma exacerbation during the course of the study

· TTF where treatment failure is defined as the first occurrence of one of the following events during the course of the study:

- Asthma exacerbation

- Clinically meaningful change in SoC asthma treatment as reported by the Investigator and confirmed by the SC

· Asthma-specific health-related quality of life as assessed by MiniAQLQ overall score

· Asthma-specific symptom scores, as assessed by the ACQ-7 and the ACT

· SoC treatments (relevant treatments, treatment characteristics, and changes in these considered clinically meaningful by the Investigator with confirmation from the SC)

· Asthma-related health care utilization defined by hospitalizations, emergency department visits, and acute care visits due to asthma and asthma-related symptoms

- Serum periostin level as assessed by both central study laboratory testing and by regional reference laboratory testing (regional reference laboratories conducting periostin testing are expected to be established in select regions later in the course of the study - see Section 4.3.9.2.1)

· FeNO

· Blood eosinophil level as assessed by both local and central study laboratory testing

· Serum IgE level as assessed by both local and central study laboratory

testing

Secondary outcome

The safety outcome measures for this study are the nature, frequency and severity of the following:

· Study assessment-related AEs

· SAEs: defined as any event that is fatal or life-threatening, results in unplanned hospitalization or prolongs an existing hospitalization, results in congenital anomaly/birth defect, or is deemed medically significant by the Investigator

· Medical events of special interest: defined as malignancies (e.g. lymphoma); infections including respiratory infections, parasitic infections such as helminthic (e.g. schistosoma infections) and protozoan (e.g. Giardia lamblia), opportunistic infections such as histoplasmosis and coccidioidomycosis, and Listeria monocytogenes infection; newly diagnosed diabetes mellitus; cataracts; bone fractures; dental operations; anaphylaxis, anaphylactoid and hypersensitivity events; and pregnancies

Exploratory Outcome Measures

The exploratory outcome measures for this study are as follows:

· Work and activity impairment as assessed by the WPAI-Asthma

· Asthma symptoms as measured by the ASUI

Study description

Background summary

Asthma is one of the most common chronic diseases in the world. It is characterized by chronic airway inflammation, bronchial hyper-responsiveness, mucus hyper-secretion and reversible airflow obstruction that result in recurrent attacks of breathlessness, chest tightness, cough and wheezing.
The relevance of molecular biomarkers as both research and clinical tools in asthma has risen with the characterization of the pathophysiological mechanisms.
Clinically amenable biomarkers of these disease processes are needed to fully exploit the potential for improvements in accurate asthma subtype diagnoses, treatment selection and monitoring of disease progress and treatment response.
Among multiple candidates, periostin presents the potential to guide each of these aspects of asthma management. Its relationship to asthma outcomes and other Th2-driven disease biomarkers merits further study in a longitudinal setting.

(see protocol page 16-18)

Study objective

The primary objective of the study is as follows:
· To compare the rate of asthma exacerbations between patients with low baseline periostin levels (< 50 ng/mL) and patients with high baseline periostin levels (* 50 ng/mL), as measured by central laboratory testing, in order to evaluate periostin as a prognostic biomarker that can identify at-risk asthmatics

The secondary objectives of the study are to assess the following:
· The prognostic value of baseline periostin levels with respect to:
- Change in pre-bronchodilator FEV1
- Time to first asthma exacerbation
- Change in FeNO
- Change in asthma-specific health-related quality of life as assessed by the Mini Asthma Quality of Life Questionnaire (MiniAQLQ)
- Change in asthma-specific symptom scores, as assessed by the Asthma Control Questionnaire-7 (ACQ-7) and the Asthma Control Test (ACT)
- Time to treatment failure (TTF)
· The prognostic value of baseline periostin levels, as measured by central laboratory testing and as measured by regional reference laboratory testing, with respect to rate of asthma exacerbations (regional reference laboratories conducting periostin testing are expected to be established in select regions later in the course of the study - see Section 4.3.9.2.1)
· The prognostic value of established risk factors measured at baseline (blood eosinophil counts, FeNO, serum IgE and history of asthma exacerbations over the 12 months prior to Visit 1) with respect to the rate of asthma exacerbations

during the study
· The prognostic value of composite measures that include baseline periostin and other established risk factors measured at baseline (i.e. blood eosinophil count, FeNO, serum IgE, history of asthma exacerbations) with respect to the rate of asthma exacerbations
· The prognostic value of baseline periostin levels in subgroups of patients (e.g. treatment subgroups such as Global Initiative for Asthma [GINA] step 4 500-1000 *g fluticasone propionate [FP], GINA step 4 >1000 *g FP, GINA step 5; geographical subgroups; or ethnic subgroups) with respect to the rate of asthma exacerbations
· The association between baseline periostin levels and clinically meaningful changes to standard of care (SoC) asthma treatment as reported by the investigator and confirmed by the study Steering Committee (SC)
- The association between periostin and other biomarker levels measured at baseline (FeNO, blood eosinophil count, serum IgE) and the rate of urgent asthma-related health care utilization over the study period
· Intra- and inter-patient variation in periostin levels, blood eosinophil counts, serum IgE levels and FeNO levels
· Variation between periostin levels, blood eosinophil counts and serum IgE levels as measured by the central laboratory versus regional reference (periostin) or local (blood eosinophils, IgE) laboratories

The safety objective of the study is to evaluate the nature, frequency and severity of the following over the study period:
· Adverse events (AEs) related to study assessments (e.g. blood draws or spirometry)
· Serious adverse events (SAEs)
· Medical events of special interest (MESIs)

The exploratory objectives for this study include, but are not limited to, assessment of the following:
· Correlation between periostin levels and key asthma biomarkers (i.e. blood eosinophil count, serum IgE, FeNO)
· Correlation of blood eosinophil count, FeNO, serum IgE and history of asthma exacerbations with rate of asthma exacerbations, FEV1, time to first asthma exacerbation, changes to SoC asthma treatment, asthma-related quality of life (assessed by the MiniAQLQ), and asthma-related healthcare utilization
· Change in asthma control, as measured by the ACQ-7 score, with respect to other biomarkers measured at baseline (i.e. FeNO, blood eosinophil count, serum IgE)
· Change in work and activity impairment, as assessed by the Work Productivity and Activity Impairment Questionnaire-Asthma (WPAI-Asthma), with respect to periostin and other biomarkers measured at baseline (i.e. FeNO, blood eosinophil count, serum IgE)
· Change in asthma symptoms, as measured by the Asthma Symptom Utility Index (ASUI) with respect to periostin and other biomarkers measured at baseline (i.e. FeNO, blood eosinophil count, serum IgE)

· Change in asthma symptoms, as measured by the Asthma Control Test (ACT) with respect to other biomarkers measured at baseline (i.e. FeNO, blood eosinophil count, serum IgE)

Study design

This is a prospective, single-arm, longitudinal, international, multicentre study in a real-world cohort of adult severe asthma patients that is being conducted to assess the relationships between asthma biomarkers and asthma-related health-outcomes.

Study burden and risks

The study assessments consist of non-invasive methods commonly used in asthma SoC (FEV1 and FeNO measurement) in addition to peripheral blood sampling and clinically applicable patient questionnaires. To reduce the burden associated with travel and time in the clinic, study evaluation days can occur within a wide temporal window (± 28 days) to increase the likelihood of coinciding with a clinic visit for standard care, and two of the five study visits will be conducted by telephone.

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

- Males and females ><=18 years of age
- Asthma diagnosed by a respiratory physician ><= 12 months prior to study enrolment
- Pre-bronchodilator forced expiratory volume in 1 second (FEV1) of 30%-85% at baseline
- Documented bronchodilator response defined as ><=12% relative improvement in FEV1 after bronchodilator administration OR a positive methacholine bronchial challenge test with PC20 (provocative concentration causing a 20% fall in FEV1) < 8 milligrams at study baseline or within 24 months prior to baseline
- Current treatment with a total daily dose of ><=500 microgram of fluticasone propionate administered by dry powder inhaler (or equivalent) and at least one of the following controller medications: long-acting beta-agonists (LABAs), leukotriene receptor antagonists (LTRAs), long-acting muscarinic antagonists (LAMAs), theophylline or oral corticosteroids; with a continued duration of at least three months prior to baseline

Exclusion criteria

- Acute or chronic parasitic, bacterial, fungal or viral infections that required, or currently require, hospitalization or antimicrobial treatment during the last four weeks
- Acute asthma exacerbation event treated with increased doses of oral or any dose of intramuscular or intravenous corticosteroids within six weeks prior to baseline
- Other relevant pulmonary diseases (e.g. chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, pulmonary arterial hypertension, tuberculosis) requiring treatment within 12 months prior to baseline
- Alcohol or substance abuse within 12 months prior to baseline
- Current smoker defined as having smoked at least one cigarette (or pipe, cigar, or marijuana) per day for >=30 days within the three months prior to baseline
- Ex-smokers with >=10 pack-year smoking history

- Treatment with omalizumab or any anti- interleukin (IL)-4, anti-IL-5, or anti-IL-13 targeted therapy currently or within six months prior to baseline
- Prior treatment with bronchial thermoplasty

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2016
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	15-09-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	11-10-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL54020.056.15