# Studying the value of fractional exhaled Nitric Oxide and blood eosinophils as biomarkers in predicting which patients will suffer from more frequent asthma exacerbations, and evaluating the subsequent healthcare resource utilisation (Assessing RIsk of exAcerbation (ARIA))

**First published:** 20/07/2017

**Last updated:** 01/04/2024

Study Finalised

## Administrative details

**EU PAS number**

EUPAS16891

**Study ID**

26465

**DARWIN EU® study**

No

**Study countries**

☐ United Kingdom

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**Study description**

5-10% of all patients presenting with asthma, have severe asthma that is refractory to standard inhaled corticosteroid (ICS) treatment. The number of blood eosinophils has been shown to be positively correlated with the frequency of severe asthma exacerbations, and is a promising marker for responsiveness to monoclonal antibody therapy in the presence of corticosteroid resistance. FeNO is another biomarker for corticosteroid responsiveness. FeNO levels and blood eosinophilia together, may predict patients with uncontrolled corticosteroid-resistant asthma who may respond positively to monoclonal antibody therapy. The study aims to correlate the level of FeNO and blood eosinophils to the number of severe exacerbations. The prospective burden of disease, healthcare resource utilisation costs, quality of life, and stability of biomarkers over time and changes in ICS dosage for patients with different categories of FeNO and blood eosinophils will also be assessed to understand their implications in severe asthma. Phase 1 and 2 primary objectives compare the rate ratio of severe exacerbations in patient groups categorised by different biomarker levels before and after FeNO measurement. Phase 3 assesses quality of life data across matched and different patient groups while phase 4 studies consistency between initial FeNo and Eosinophil levels to those taken at specialist clinics. A bespoke dataset(OPCRD) of FeNO and blood eosinophil measurements from asthmatic patients in the UK is used. 850 patients between the 6 groups for phase 1 and 2 are required. Matched analysis will take place between 2 groups of groups of interest identified analysis. Primary analysis will be carried with numbers of exacerbations collected and then compared across matched groups.Results will be presented additionally as a rate ratio between comparison groups.

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**Study status**

Finalised

# Research institutions and networks

## Institutions

### Observational & Pragmatic Research Institute Pte (OPRI)

United Kingdom

**First published:** 06/10/2015

**Last updated:** 19/08/2024

**Institution** **Educational Institution** **Laboratory/Research/Testing facility** **ENCePP partner**

## Networks

### Optimum Patient Care (OPC) Network

United Kingdom (Northern Ireland)

**First published:** 26/09/2015

**Last updated:** 16/06/2025

**Network** **ENCePP partner**

## Contact details

**Study institution contact**

David Price dprice@opri.sg

Study contact

dprice@opri.sg

**Primary lead investigator**

David Price

Primary lead investigator

## Study timelines

**Date when funding contract was signed**

Planned: 13/12/2016

Actual: 13/12/2016

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**Study start date**

Planned: 20/12/2016

Actual: 20/12/2016

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**Data analysis start date**

Planned: 27/12/2016

Actual: 27/12/2016

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**Date of final study report**

Planned: 13/08/2017

Actual: 22/06/2017

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

AstraZeneca

## Study protocol

121216 FeNO and Eosinophils in ICS-Treated Asthma_v1.3.pdf (1.19 MB)

## Regulatory

**Was the study required by a regulatory body?**

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Methodological aspects

## Study type

## Study type list

**Study topic:**

Disease /health condition

Other

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**Study topic, other:**

Disease/Epidemiology study

**Study type:**

Non-interventional study

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**Scope of the study:**

Other

**If ‘other’, further details on the scope of the study**

Medication use Characterisation

**Data collection methods:**

Secondary use of data

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**Main study objective:**

The aim of the study is to correlate the level of FeNO and blood eosinophils to the number of severe exacerbations. Assessment of both biomarkers together may provide a novel method to identify patients at higher risk of exacerbations and may benefit from monoclonal antibody treatment.

## Study Design

**Non-interventional study design**

Cohort

## Population studied

**Short description of the study population**

Patients with asthma and who were registered at a general practice which provides data to Optimum Patient Care (OPC).
Patients with following criteria were included:
1. A diagnostic Read code for asthma (ever, without an asthma resolution Read code at the index date) qualifying for inclusion in the register of patients with asthma, maintained by GPs for the Quality Outcomes Framework (QOF) OR prescription of ≥2 asthma related medications, one of which must be an ICS, none of which are a LAMA, and without a FEV1/FVC<0.70
2. A FeNO reading in the last 2 years prior to the extraction date that serves as the index date
3. ≥ 1 prescription for ICS in the year prior to the most recent FeNO reading
4. Age 18-80 inclusive at the date of the most recent FeNO reading
5. ≥ 1 valid blood eosinophil count measurement within 2 years prior to the index date
6. Continuous data prior to index date for one year
7. Completion of relevant QoL questionnaire (phase 3)
8. Attendance and completion of asthma review clinic (phase 4)

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**Age groups**

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

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**Special population of interest**

Other

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**Special population of interest, other**

Asthma patients

**Estimated number of subjects**

850

# Study design details

**Outcomes**

Phase 1 primary objective:To find the rate ratio of severe exacerbations in patients categorised by different biomarker levels in the year prior to the FeNO measurement. Phase 1 secondary objective:To describe demographic characteristics, lung function, comorbidities, respiratory medication and healthcare resource utilisation in patients categorised by biomarkers.

**Data analysis plan**

A characterisation of all baseline demographic, co-morbidity, indicators of disease severity and other patient characteristic variables will be carried out and presented for each arm. Potential confounders are identified based on a combination of baseline imbalance, bias potential and expert judgement, and the most relevant confounders will be used for direct matching.The primary analysis will be carried out in accordance after matching, and will require the numbers of exacerbations to be collected and then compared through matched groups, with the exact matching method based on baseline characteristics collected through the secondary analysis. Results will be presented additionally as a rate ratio between comparison groups.Secondary Analysis,descriptive statistics will be carried out in accordance with the general methods. Characteristics of cohorts will be compared using the chi-squared test and the Kruskal Wallis test, as appropriate for unmatched groups.

# Documents

**Study report**

2017_06_22_AUREA_final_report_1.2FIN.pdf (5.14 MB)

# Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s)**

Optimum Patient Care Research Database

**Data sources (types)**

Electronic healthcare records (EHR)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

Unknown