# Triple therapy effectiveness in COPD patients with characteristics of asthma: A pragmatic primary care trial - The TRACkER trial

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It is expected that patients in the triple therapy group improve their health status (CCQ score) more than the patients in the LABA/LAMA group.

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| **Ethical review** | Positive opinion |
| **Status** | Recruiting |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON28851

**Source**
NTR

**Brief title**
TRACkER

**Health condition**

COPD

### Sponsors and support

**Primary sponsor:** GPRI
**Source(s) of monetary or material Support:** Chiesi Pharamceuticals B.V.

### Intervention

## Outcome measures

### Primary outcome

To investigate the effectiveness of triple therapy (ICS/LABA/LAMA) on the change in health status, measured with the Clinical COPD Questionnaire (CCQ), in symptomatic ICS-naive COPD patients with characteristics of asthma according to GOLD 2019 (age of onset, pattern of respiratory symptoms, history/family of asthma, history of Atopy) and blood eosinophil counts of ≥100 cells per µL compared to treatment with dual therapy (LABA/LAMA), within a primary care population. Effectiveness is regarded as difference in the proportion of patients a with minimal clinically improvement on health status (CCQ improvement ≥0.4) between the study groups.

### Secondary outcome

- To identify patient and disease characteristics that are predictive for triple therapy effectiveness. Effectiveness is defined as improvement in CCQ of ≥0.4 from baseline to follow-up.The patient and disease characteristics that will be assessed are the following: 1) Patient demographics and disease history; 2) Symptoms of asthma as defined by GOLD 2019; 3) Blood test outcome measures (specific IgE and eosinophil counts); 4) Spirometry outcome measures; 5) Fractional exhaled nitric oxide (FeNO) levels; 6) Asthma Control Questionnaire (ACQ); 7) Small Airways Dysfunction Test (SADT) - To compare the number of moderate and severe exacerbations before (6 months) and during the study (6 months) between the study groups. - To investigate the difference in the pneumonia incidences between the study groups - To compare the proportion of net responders (positive responders (≥0.4 improvement on the CCQ) minus negative responders (≤0.4 decline on the CCQ)) between the study groups. - To compare the proportion of patients with clinically relevant improvement on either one or both, the CCQ (≥0.4) or the ACQ (≥0.5). - To compare the properties of the CCQ and the COPD Assessment Test (CAT) over the study period. - To compare the difference in lung function measures, Eos and FeNO between the study groups. - To describe patient reported side effects using the Inhaled Corticosteroids side-effect Questionnaire Short Form (ICQ-S). - To collect health resource utilization data (e.g. exacerbations, hospitalizations) and investigate the difference in health resource use and costs between the study groups. - To investigate the differences in genome-wide expression of mRNA, MiRNA and methylation status in epithelial cells derived from nasal brushings between the study groups.

# Study description

### Background summary

Rationale: (Inter)National guidelines identify several patient characteristics that can be used to select patients with Chronic Obstructive Pulmonary Disease (COPD) who may benefit from inhaled corticosteroids (ICS) containing treatment. These characteristics include asthma

characteristics, high blood eosinophil (Eos) counts and frequent exacerbations (despite the usage of a bronchodilator). However, this evidence was originally based on post hoc analysis from randomised controlled trials. Little is known regarding the utility of these characteristics in real life, as tools for guiding doctor's decision to prescribe ICS containing medication in routine practice. Objective: To investigate the effectiveness of triple therapy (ICS/ long-acting beta 2 agonist (LABA)/long-acting muscarine antagonist (LAMA)) on the change in health status, measured with the Clinical COPD Questionnaire (CCQ), in symptomatic ICS-naive COPD patients with characteristics of asthma according to GOLD 2019 and blood eosinophil counts of ≥100 cells per µL compared to treatment with dual therapy (LABA/LAMA), within a primary care population. Effectiveness is regarded as difference in the proportion of patients with a minimal clinically improvement on health status (CCQ improvement ≥0.4) between the study groups. Study design: This is a prospective, real-life, randomised controlled trial of 26 weeks, which is conducted in general practices in the north of the Netherlands comparing triple therapy (ICS/LABA/LAMA) with dual bronchodilator treatment (LABA/LAMA). We aim to randomise 316 patients. Patients will be randomized (1/1) either to the triple therapy arm or the LABA/LAMA treatment arm. Study population: ICS-naive symptomatic (CCQ≥1) primary care COPD patients aged over 40 years who are currently using one or two long-acting bronchodilators with characteristics of asthma (age of onset <20 years; day to day variation in symptoms or symptoms which are worse during the night/early morning; history of asthma, allergy, rhinitis, eczema) and a blood eosinophil count of ≥100 cells per µL. Intervention: In the intervention group patients will use a single inhaler triple therapy (Trimbow), which includes a combination of beclomethasone dipropionate, formoterol fumarate dihydrate, and glycopyrronium bromide. This inhaler is used twice a day. In the control group patients will use dual bronchodilator treatment (LABA/LAMA) which is used according to the prescription. Main study parameters/endpoints: The primary outcome of this study is the difference in the proportion of patients with a clinically relevant improvement in health status (≥0.4 improvement on the CCQ) between the triple therapy group and LABA/LAMA treatment groups at the end of the 26 weeks intervention period. All main analyses will be conducted intention-to-treat.

## Study objective

It is expected that patients in the triple therapy group improve their health status (CCQ score) more than the patients in the LABA/LAMA group.

## Study design

Study start: 02-12-2019 Start inclusion: 16-12-2019 Study period: 26 weeks/6 months End inclusion period: 01-07-2019

## Intervention

In the intervention group patients will use a single inhaler triple therapy (Trimbow), which includes a combination of beclomethasone dipropionate, formoterol fumarate dihydrate, and glycopyrronium bromide. This inhaler is used twice a day. In the control group patients will use dual bronchodilator treatment (LABA/LAMA) which is used according to the prescription.

# Contacts

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# Eligibility criteria

## Inclusion criteria

- Physician diagnosis of COPD (documented obstruction or obstruction measured at the first study visit) - Age 40 years and older - Symptomatic (defined as Clinical COPD Questionnaire score ≧ 1) - ICS-naive (last 12 months no ICS containing treatment) - Usage of a long-acting bronchodilator; either usage of a single LABA or LAMA, usage of a single LABA and a single LAMA, or a usage of a single LABA/LAMA inhaler. Patients are allowed to use short-acting bronchodilator. - Blood eosinophils ≥100 cells per µL - One or more characteristics of asthma according to GOLD 2019 (age of onset, pattern of respiratory symptoms, history/family of asthma, history of Atopy).

## Exclusion criteria

- Chronic oral corticosteroid, use more than 60 days in the last 3 months - Recent exacerbation (last 6 weeks before inclusion) - Life expectancy of less than 2 years - Allergy to intervention formulation - Inability to understand Dutch - Any other condition which, at the GPs and/or investigator’s discretion, is believed to present a safety risk or may impact the study results - Patients participating in another ongoing clinical trial that in the investigator’s opinion influences the current study (e.g. another randomized controlled trial) - In ability to understand and sign the written consent form.

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 02-12-2019 |
| Enrollment: | 316 |
| Type: | Anticipated |

## IPD sharing statement

**Plan to share IPD:** Yes

**Plan description**
The researchers can be contacted to discuss the details of sharing the data.

# Ethics review

Positive opinion

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| Date: | 11-12-2019 |
| Application type: | First submission |

# Study registrations

## Followed up by the following (possibly more current) registration

ID: 54789
Bron: ToetsingOnline
Titel:

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

No registrations found.

## In other registers

| Register | ID |
|---|---|
| NTR-new | NL8227 |
| CCMO | NL71310.056.19 |

# Study results