Triple therapy effectiveness in COPD patients with characteristics of asthma: A pragmatic Primary Care trial - The TRACkER trial

Published: 29-11-2019
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This study has been transitioned to CTIS with ID 2023-508300-37-00 check the CTIS register for the current data. To investigate the effectiveness of triple therapy (ICS/ long-acting beta 2 agonist (LABA)/long-acting muscarine antagonist (LAMA)) on…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON54789

Source
ToetsingOnline

Brief title
TRACkER

Condition

- Bronchial disorders (excl neoplasms)

Synonym
COPD

Research involving
Human

Sponsors and support

Primary sponsor: GPRI

Source(s) of monetary or material Support: Chiesi Farmaceutici,Chiesi Pharamceuticals B.V.

Intervention

Keyword: COPD, Pragmatic, Primary Care, Triple therapy

Outcome measures

Primary outcome

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.

Secondary outcome

Additionally, we aim to 1) identify characteristics that predict positive additional response to triple therapy above dual bronchodilator therapy. Effectiveness is defined as improvement in CCQ of >=0.4 from baseline to follow-up.; 2) To compare the number of moderate and severe exacerbations before (6 months) and during the study (6 months) between the study groups; 3) compare the proportion of patients with clinically relevant improvement on either CCQ (>=0.4) or ACQ (>=0.5) between the study groups; 4) 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; 5) compare the difference in lung function measures, Eos and FeNO between the study groups; 6) describe the patient reported side effects using the inhaled corticosteroids side-effects questionnaire Short Form (ICQ-S); 7) investigate

the difference in health resource use and costs between the study groups; 8) investigate the differences in genome-wide expression of ribonucleic acid (RNA) (messenger (mRNA) and micro (MiRNA)) and methylation status in epithelial cells derived from nasal brushings between the study groups; 9) compare the properties of the CCQ and the COPD Assessment Test (CAT) over the study period;10) investigate the difference in the pneumonia incidences between the study groups; 11) validate the role of matrix proteins in the pathological processes in COPD to identify therapeutic targets for intervention and examine their utility as biomarkers for monitoring and predicting disease progression and/or treatment response between the study group between the study groups; 12) investigate whether presence of a single nucleotide polymorphisms (SNPs) or combination of SNPs can a) help to predict if COPD patients respond favorably to ICS, and b) influence expression level of a COPD relevant gene, i.e. are expression quantitative trait loci.

Study description

Background summary

(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 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.

Study objective

This study has been transitioned to CTIS with ID 2023-508300-37-00 check the CTIS register for the current data.

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). 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. Additionally, we aim to 1) identify characteristics that predict positive additional response to triple therapy above dual bronchodilator therapy. Effectiveness is defined as improvement in CCQ of >=0.4 from baseline to follow-up; 2) To compare the number of moderate and severe exacerbations before (6 months) and during the study (6 months) between the study groups; 3) compare the proportion of patients with clinically relevant improvement on either CCQ (>=0.4) or ACQ (>=0.5) between the study groups; 4) 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; 5) compare the difference in lung function measures, Eos and FeNO between the study groups; 6) describe the patient reported side effects using the inhaled corticosteroids side-effects questionnaire Short Form (ICQ-S); 7) investigate the difference in health resource use and costs between the study groups; 8) investigate the differences in genome-wide expression of ribonucleic acid (RNA) (messenger (mRNA) and micro (MiRNA)) and methylation status in epithelial cells derived from nasal brushings between the study groups; 9) compare the properties of the CCQ and the COPD Assessment Test (CAT) over the study period;10) investigate the difference in the pneumonia incidences between the study groups; 11) validate the role of matrix proteins in the pathological processes in COPD to identify therapeutic targets for intervention and examine their utility as biomarkers for monitoring and predicting disease progression and/or treatment response between the study group between the study groups; 12) investigate whether presence of a single nucleotide polymorphisms (SNPs) or combination of SNPs can a) help to predict if COPD patients respond favorably to ICS, and b) influence expression level of a COPD relevant gene, i.e. are expression quantitative trait loci.

Study design

This is a prospective, real-life, randomised controlled trial of 26 weeks, which is conducted in general practices and hospitals 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 randomised (1/1) either to the triple therapy arm or the LABA/LAMA treatment arm.

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.

Study burden and risks

Participating in the study requires two visits to the patient*s primary care practice/hospital. One at the start of the study and one after 26 weeks. During both visits* patients will be requested to complete questionnaires and perform lung function tests. Additionally, blood eosinophil counts are measured using a point-of-care test (finger prick) and if consented by the patient a nasal brushing is performed. At the first visit patients are referred to a location of the primary care laboratory for an IgE blood test. In the end, it is expected that triple therapy reduces respiratory symptoms and the number of exacerbations and hospitalizations in COPD patients. Pneumonia has been reported as a common, major side effect of ICS in COPD patients. However, this applies to COPD patients in general, it is not known if pneumonia frequently occurs in COPD patients with asthma characteristics (our study population).

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

- 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 AND one or more characteristics of asthma according to GOLD 2019.

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)
- Inability to understand and sign the written consent form

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2020
Enrollment:	316
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Beclomethasone dipropionate/formoterol fumarate dihydrate/glycopyrronium bromide
Generic name:	Triple therapy
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-11-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2023
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

ID: 28851
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EU-CTR	CTIS2023-508300-37-00
EudraCT	EUCTR2019-003351-11-NL
CCMO	NL71310.056.19

Study results

Date completed: 19-02-2024

Summary results
Trial ended prematurely