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Is there a maximum effect of fixed triple combination therapy to treat chronic obstructive pulmonary disease (COPD)?

Submission date
17/09/2020

Recruitment status
No longer recruiting

Registration date
22/09/2020

Overall study status
Completed

Last Edited
17/06/2021

Condition category
Respiratory

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation caused by abnormalities in the lungs due to exposure to particulate matter or gas. Treatment with inhaled corticosteroids (ICS) in combination with long-acting bronchodilators (to open the air passages in the lungs) is more effective than the individual components in improving lung function, symptoms, and exacerbations. Usually, a triple combination with one ICS plus two long-acting bronchodilators are administered at severe COPD patients. Adding a short-acting bronchodilator (i.e. salbutamol) in addition to basic inhalation therapy with long-acting bronchodilators may further improve the level of bronchodilation. The aim of this study was to assess whether triple combination therapy may lead to maximal bronchorelaxant effect in the airways of COPD patients.

Who can participate?
Severe COPD patients were enrolled in the study.

What does the study involve?
Patients were treated for 15 days with triple combination therapy, and generally they were assessed for lung function, symptoms, and routine procedures.

What are the possible benefits and risks of participating?
These patients had the benefit to be treated with the most effective therapy for severe COPD, the so-called triple combination therapy. The risks were the potential adverse events already known for the triple combination therapy used in this study and already approved in the market, named Trimbow®.

Where is the study run from?
The study was run at the University Hospital of Rome "Tor Vergata", Italy,

When is the study starting and how long is it expected to run for?
January 2019 to September 2020

Who is funding the study?
The University Hospital of Rome "Tor Vergata" (Italy)

Who is the main contact?
Prof. Paola Rogliani
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
252/19

Study information

Scientific Title
Ceiling effect of triple beclomethasone dipropionate/formoterol fumarate/glycopyrronium bromide combination in COPD: a translational bench-to-bedside study

Study objectives
The aim of this study is to assess residual bronchodilation in patients suffering from chronic obstructive pulmonary disease (COPD) after administration of the beclomethasone dipropionate (BDP)/formoterol fumarate (FF)/glycopyrronium bromide (GB) triple combination. BDP/FF/GB is a fixed-dose combination (FDC) of a long-acting muscarinic antagonist (LAMA), a long-acting β2 adrenoceptor agonist (LABA) and an inhaled corticosteroid (ICS) already approved as chronic therapy by EMA and AIFA for COPD patients with two moderate exacerbations per year or one severe and symptomatic exacerbation. According to the current GOLD recommendations, the COPD patient in chronic therapy with bronchodilators can use, if needed, therapy with short-acting bronchodilators such as salbutamol. However, to date, it is not known whether the "add-on" therapy of a short-acting bronchodilator such as salbutamol may result in an improvement in lung function in COPD patients already on BDP/FF/GB therapy.

Overall, this study investigates whether BDP/FF/GB may lead to ceiling bronchorelaxant effect in the airways of COPD patients, and whether there may be some different effect at the level of medium bronchi and small airways.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/02/2020, Local institutional ethics committee CEI (Comitato Etico Indipendente, Rome “Tor Vergata”, Viale Oxford, 81 - 00133 Roma, Italy; +39 06 2090 0035; no email provided), ref: RS 252/19, 2020

Study design
Pilot single-arm open-label prospective observational single-centre study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD)

Interventions
Pulmonary function test (PFT) and impulse oscillometry (IOS) are performed at baseline before and during dose-response curve (DRC) to salbutamol (100 µg, 200 µg, 400 µg, 800 µg). After that, patients are treated with Trimbow®, an extrafine formulation of BDP, FF, and GP (BDP/FF/GB 100/6/12.5 µg) administered BID as FDC. At day 14 the DRC to salbutamol is performed on top of the peak effect induced by BDP/FF/GB 100/6/12.5 µg FDC (2 h after the last inhalation of the FDC), along with PFT and IOS. At day 15 (visit 4) the DRC to salbutamol is performed on top of the trough effect induced by BDP/FF/GB 100/6/12.5 µg FDC (11 h after the last inhalation of the triple combination therapy), along with PFT and IOS.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
1. Beclomethasone dipropionate 2. Formoterol fumarate 3. Glycopyrronium bromide 4. Salbutamol

Primary outcome(s)
Bronchorelaxant effect at the level of small airways (airway resistance) measured using impulse oscillometry at baseline (day 1), day 14 and day 15

Key secondary outcome(s))
1. Bronchorelaxant effect at the level of medium bronchi measured using forced expiratory volume in 1 s [FEV1] at baseline (day 1), day 14 and day 15
2. Dyspnea using Modified British Medical Research Council Questionnaire (mMRC) and Visual Analogue Scale (VAS) at baseline (day 1), day 14 and day 15
3. Oxygen saturation (SpO2) and heart rate (HR) using pulse oximetry at baseline (day 1), day 14 and day 15

Completion date
01/09/2020

Eligibility

Key inclusion criteria
1. COPD patients ≥40 years old
2. Current or former smokers, with a cigarette smoking history of ≥10 pack-years
3. Confirmed diagnosis of COPD (FEV1/forced vital capacity (FVC) <0.7) FEV1 <65% predicted, history of ≥1 severe exacerbation of COPD in the last year

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
16

Key exclusion criteria

1. Patients with history of asthma
2. Reversibility of FEV1 by >200 ml and/or >12% after inhalation of 200 µg salbutamol
3. Under treatment with ICS

Date of first enrolment
27/02/2020

Date of final enrolment
30/07/2020

Locations

Countries of recruitment
Italy

Study participating centre
University of Rome "Tor Vergata"
Italy
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Sponsor information

Organisation
University of Rome Tor Vergata

ROR
https://ror.org/02p77k626

Funder(s)

Funder type
University/education

Funder Name
Università degli Studi di Roma Tor Vergata

Alternative Name(s)
University of Rome Tor Vergata

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Italy

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
Investigator: Paola Rogliani paola.rogliani@uniroma2.it
Type of data: patient-level data, available in about 6 months for about 12 months
Data will be available on request by providing anonymized excel files.
Data will be available only for reasonable scientific research and shared with scientific institutions, only after approval by the local Ethics Committee.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		12/06/2021	17/06/2021	Yes	No