

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

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<b>Registration date</b> 22/09/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 17/06/2021	<b>Condition category</b> Respiratory	<input type="checkbox"/> 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  
paola.rogliani@uniroma2.it

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Paola Rogliani

**Contact details**  
Via Montpellier, 1  
Rome  
Italy  
00133  
+39 (0)6 2090 4656  
paola.rogliani@uniroma2.it

**Type(s)**  
Scientific

**Contact name**  
Dr Luigino Calzetta

**Contact details**  
Via Montpellier, 1  
Rome  
Italy  
00133  
+39 (0)6 76259 6666  
luigino.calzetta@unipr.it

## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**ClinicalTrials.gov (NCT)**  
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  $\beta_2$  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  $\mu$ g, 200  $\mu$ g, 400  $\mu$ g, 800  $\mu$ g). After that, patients are treated with Trimbrow®, an extrafine formulation of BDP, FF, and GP (BDP/FF/GB 100/6/12.5  $\mu$ g) 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  $\mu$ g 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  $\geq 40$  years old
2. Current or former smokers, with a cigarette smoking history of  $\geq 10$  pack-years
3. Confirmed diagnosis of COPD (FEV1/forced vital capacity (FVC)  $< 0.7$ ) FEV1  $< 65\%$  predicted, history of  $\geq 1$  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

00133

**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](mailto: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?
<a href="#">Results article</a>		12/06/2021	17/06/2021	Yes	No