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129Xe MRI study of single triple therapy inhaler effects in COPD patients with persistent, moderate-severe dyspnea and/or poor health status with high or low risk of flare-up.

Submission date 04/11/2025	**Recruitment status** Recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 04/11/2025	**Overall study status** Ongoing	
Last Edited 04/11/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
This study is looking at the effects of a triple therapy medication (Fluticasone/Umeclidinium /Vilanterol) using magnetic resonance imaging (MRI). This medication is delivered through a device called an Ellipta inhaler. It contains three types of medications normally used to treat COPD. Fluticasone is an inhaled corticosteroid (ICS), which reduces inflammation (swelling) in the airways. Umeclidinium is a long-acting muscarinic antagonist (LAMA), which opens up the airways. Vilanterol is a long-acting beta-2-agonist (LABA), which also opens up the airways.
The goal of this study is to determine whether switching from your current medication to this triple therapy improves your lung imaging measurements, lung function, and quality of life as measured by questionnaires and disease flare-ups. This triple therapy medication has been approved by Health Canada to treat COPD.
The purpose of this study is to determine the effects of this triple therapy inhaler on you and your COPD using:
• Breathing tests
• A type of MRI that measures lung function
• A chest CT (computed tomography) that measures lung structure
• Questionnaires that measure COPD control and quality of life

Who can participate?
You may be eligible for this study if:
• You are 50 to 85 years old
• You are able and willing to provide written informed consent
• You are able and willing to follow the study protocol
• Your COPD is considered stable for at least 3 months
• During the screening visit you have elevated questionnaire results or a FEV1 lower than 80% of your predicted value

What does the study involve?
Participants will attend 2 in-person study visits over a period of 12 weeks. There is also 1 optional visit at Week 48 (or approximately 1 year after the first visit). Each in-person study visit will take approximately 2-3 hours. Vital signs will be recorded at the beginning of the visit. Lung tests and an MRI scan will be performed before and after inhaling four puffs (100 mcg each) of a bronchodilator and quietly resting for 15 minutes. CT will be acquired after post-bronchodilator MRI. Questionnaires will be completed after post-bronchodilator assessments are completed. The six-minute walk test (6MWT) will be performed after all other testing is complete.

What are the benefits and possible risks of participating?
This medication is approved for use in COPD and is available outside of this study so benefits of taking triple therapy medication would not be study specific. Information learned from this study may help us better understand this medication and how it affects your lungs and may help other people with COPD in the future. It is possible that you will not benefit from participating in the study.
You may feel discomfort during some of these tests and some may have risks, such as:
• Spirometry breathing tests may result in shortness of breath and light-headedness.
• Tests done in the body plethysmograph may cause claustrophobia, nausea, or vomiting.
• You may experience side effects related to the salbutamol (Ventolin). The most common adverse reactions to salbutamol (3-14%) are throat irritation, viral respiratory infections, upper respiratory inflammation, cough, and musculoskeletal pain. Less common side effects (1-3%) are diarrhea, laryngitis, tachycardia (increased heart rate), palpitation and dizziness.
• When you do blood tests, a needle will be used to puncture the skin. When the skin is punctured, there is always a very small chance of introducing an infection into the body. If you notice a fever, persistent redness or persistent pain at the injection site, please follow up with your physician to rule out an infection.
• The CT delivers a radiation dose to your lungs, the mean total effective dose is approximately 1.4 mSv per scan. The cancer risk related to this radiation dose is the same as the cancer risk related to smoking 23 cigarettes over a lifetime and about half the annual natural background radiation in London, Ontario.
• There are no known biological risks associated with MR imaging. Some people cannot have an MRI because they have some type of metal in their body. For instance, if you have a heart pacemaker, artificial heart valves, metal implants such as metal ear implants, bullet pieces, chemotherapy or insulin pumps, or any other metal such as metal clips or rings, you cannot have an MRI. During this test, you will lie in a small, closed area inside a large magnetic tube. Some people may get scared or anxious in small places (claustrophobic). An MRI may also cause possible anxiety for people due to the loud banging made by the machine and the confined space of the testing area. You will be given earplugs to help reduce the noise.
• You may feel short of breath or fatigued from the six-minute walk test. You may stop and rest periodically if this happens during the test.
• We maintain a database to link your personal identifiers to your unique database ID. These electronic records are stored on an internal firewall protected server, located in a secured server room at Robarts Research Institute. There is a very small chance of a security breach that could then link your study ID with your personal identifiers.

Where is the study run from?
Robarts Research Institute, Western University (Canada)

When is the study starting and how long is it expected to run for?
November 2025 to October 2028

Who is funding the study?
GlaxoSmithKline (USA)

Who is the main contact?
Grace Parraga, PhD, gparraga@uwo.ca

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Grace Parraga

ORCID ID
https://orcid.org/0000-0002-5619-4145

Contact details
Western University
Robarts Research Institute, Rm. 5135
1151 Richmond St.
London
Canada
N6A 5B7
+1-519-931-5265
lungimaging@uwo.ca

Additional identifiers

ClinicalTrials.gov (NCT)
NCT07192016

Study information

Scientific Title
Mechanistic 129Xe MRI study of single inhaler FF/UMEC/VI effects in COPD patients with persistent, moderate-severe dyspnea and/or poor health status with high or low risk of exacerbation (MUST)

Acronym
MUST

Study objectives
To measure the effect of 12-weeks daily (and optional 48-weeks) single inhaler triple therapy on 129Xe MRI Ventilation Defect Percent (VDP) with fluticasone furoate/umeclidinium/vilanterol (100/62.5/25 µg) delivered via Ellipta inhaler in COPD patients

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/10/2025, Western Research Ethics Board (Office of Human Research Ethics, Rm 5150, Support Services Building, Western University, London, N6G 1G9, Canada; +1-519-661-3036; wrem@uwo.ca), ref: Project ID 127775

Primary study design
Interventional

Study design
Single centre open-label no control arm two treatment subgroups

Study type(s)
Treatment

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

Interventions
All participants will receive once daily FF/UMEC/VI (100/62.5/25 µg) via single Ellipta inhaler, starting at the end of visit 1, for 12-weeks (and optional 48-weeks)

Intervention Type
Drug

Phase
Phase III/IV

Drug/device/biological/vaccine name(s)
fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) 100/62.5/25 ug in a single Ellipta inhaler-Trelegy

Primary outcome(s)
Effect of FF/UMEC/VI (100/62.5/25 ug) measured using 129Xe MRI ventilation defect percent (VDP) and FEV1 after 12-weeks therapy (Visit-2) and optional 48-weeks (Visit-3) therapy

Key secondary outcome(s)
1. Lung function/volume at Visit-2 (and optional Visit-3)
2. SGRQ, CAT, mMRC scores as well as 6MWD
3. Blood/CT measurements of type 2 inflammation
4. Baseline VDP and delta VDP at 12-weeks
5. Exacerbation rate measured using the number of exacerbations over the total patient years, measured from study start

Completion date
31/10/2028

Eligibility

Key inclusion criteria

1. Patient understands study procedures and is willing to participate in the study as indicated by the patient's signature.
2. Provision of written, informed consent prior to any study specific procedures.
3. Males and females 50-85 years of age.
4. Stable COPD, currently on dual therapy LAMA/LABA or ICS/LABA or initial maintenance therapy for at least 3 months.
5. mMRC score ≥2 and/or CAT score ≥10
6. Low risk subgroup: participant has experienced ≤1 exacerbation in the past year and no hospitalizations for COPD.
High risk subgroup: participant has experienced ≥2 exacerbations in the past year.
7. Female of childbearing potential (after menarche) must ensure that they are using an effective form of birth control for at least 2 months prior to each imaging visit, throughout the duration of the study, and 8 weeks after last dose of study drug, with negative urine pregnancy test taken within 24 hr of any planned CT examination at Visit-1 through Visit-3. Examples of effective birth control include:
a. True sexual abstinence
b. A vasectomized sexual partner
c. Implanon®
d. Female sterilization by tubal occlusion
e. Effective intrauterine device (IUD)/levonogestrel intrauterine system (IUS)
f. Depo-Provera™ injections
g. Oral contraceptive
h. Evra Patch™
i. Nuvaring™
8. Female permanently sterile due to: 1) documented hysterectomy, 2) documented bilateral salpingectomy, and 3) documented bilateral oophorectomy.
9. Postmenopausal female: defined as female with no menses for 12 months without an alternative medical cause.
10. Male participants who are sexually active with a woman who can still have children, must agree to use a double barrier method of contraception (male condom with diaphragm or male condom with cervical cap) from the first dose of the study drug until 8 weeks after last dose.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 Years

Upper age limit
85 Years

Sex
All

Total final enrolment
60

Key exclusion criteria
1. Patient has an implanted mechanically, electrically, or magnetically activated device or any metal in their body which cannot be removed, including but not limited to pacemakers, neurostimulators, biostimulators, implanted insulin pumps, aneurysm clips, bioprosthesis, artificial limb, metallic fragment or foreign body, shunt, surgical staples (including clips or metallic sutures and/or ear implants) (at the discretion of the MRI Technologist).
2. In the investigator's opinion, participant suffers from any physical, psychological or other condition(s) that might prevent performance of the MRI or CT, such as severe claustrophobia.
3. Participants who are pregnant, breastfeeding or have a positive pregnancy test at initial screening visit.
4. Participant is unable to perform spirometry or plethysmography maneuvers.
5. Participant is unable to perform MRI and CT breath-hold maneuvers.
6. Participant has an unstable cardiovascular, gastro-intestinal, hepatic, renal, neurologic, metabolic or psychiatric disease.
7. Participation in any clinical trial of an investigational agent or procedure within three months prior to screening or during the study.
8. Known history of allergy or reaction to the study drug formulation.
9. Participant has a blood pressure of >150 mmHg systolic or >95 mmHg diastolic on more than 2 measurements done >5 minutes apart at Visit-1.
10. Participants with a recently (<2 months) documented diagnosis of asthma.

Date of first enrolment
20/11/2025

Date of final enrolment
31/10/2028

Locations

Countries of recruitment
Canada

Study participating centre
Robarts Research Institute, Western University
1151 Richmond Street
London
Canada
N6A 5B7

Sponsor information

Organisation

University of Western Ontario

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

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
gparraga@uwo.ca

IPD sharing plan summary
Available on request