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Maintaining the integrity of muscle during hospitalisation in older persons with severe acute exacerbation of chronic obstructive pulmonary disease (MINT-COPD)

Submission date
24/01/2025

Recruitment status
Recruiting

Registration date
09/04/2025

Overall study status
Ongoing

Last Edited
03/02/2026

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
People living with Chronic Obstructive Pulmonary Disease (COPD) experience "flare-ups", which can result in admission to hospital and loss of muscle function. This research study is testing a new unlicensed medication called RJx-01 and aims to assess its safety and tolerability, along with its impact on muscle function and quality of life. Participants will take the medication for 6-months, starting when they are in hospital. At monthly appointments, we will conduct safety and muscle function tests.
RJx-01 is made of two medicines, metformin (used for diabetes) and galantamine (used for dementia), combined into a new treatment. Participants in this study will either receive RJx-01 or a placebo (a “dummy drug”) to compare the effects. The study will check how safe the treatment is, how well it is tolerated, and its effect on muscle health and quality of life.

Who can participate?
Patients aged 45 years and over admitted to the hospital with COPD

What does the study involve?
Participants will be randomly assigned to receive either RJx-01 or a placebo (a "dummy" treatment) in daily sachets for 168 days, starting when they leave the hospital. During this period, participants will be asked to attend monthly follow-up visits at Glenfield Hospital's Respiratory Biomedical Research Centre. At each visit, participants will receive more of their assigned treatment and have their health monitored through tests on breathing, muscle strength, body composition, blood, sputum (mucus), and urine samples.

What are the possible benefits and risks of participating?
Participation is voluntary, and participants can choose to stop at any time without affecting their standard medical care. This trial is organised by the University of Leicester and Rejuvenate Biomed, funded by the Wellcome Leap Dynamic Resilience Program. The findings will help to understand the potential of RJx-01 as a new treatment option for COPD patients to preserve

muscle health and improve recovery after hospital admissions. Results will be published, but personal information will remain confidential and anonymised.
RJx-01 has already been trialled in healthy volunteers, where the treatment was well tolerated and showed a positive effect on muscle strength. However, these effects have not yet been explored in patients. The two active ingredients of RJx-01, Metformin and Galantamine, are individually licensed in the United Kingdom. Metformin has been used for decades as the first-line treatment of type 2 diabetes, and Galantamine has been used for many years for the treatment of Alzheimer's disease. As a result, the safety of these two medications on their own is well understood.
As of October 2024, there is limited information on the safety of taking of Metformin and Galantamine together. However, product information for both Metformin and Galantamine does not restrict the use of both medications at the same time. Because they do not act on the same primary pathways in the body, it is unlikely that taking one would have a negative impact on the effects of the other.
On their own, there are risks associated with both Metformin and Galantamine. For Metformin, risks include lactic acidosis and the occurrence of gastrointestinal (GI) side effects such as diarrhea. Lactic acidosis is a very rare but serious life-threatening condition where too much lactic acid builds up in the body, leading to a drop in blood pH (acidosis). Metformin-associated lactic acidosis (MALA) can occur due to conditions like renal or liver failure, circulatory dysfunction, or an increased production of lactate from issues such as hypoxia or severe infection.
The risk for MALA occurring in study subjects is lowered by limiting the highest Metformin dose to 960 mg/day, by excluding subjects with renal or hepatic failure and excluding those with significant circulatory dysfunction or (heart failure, sepsis, shock, severe dehydration, alcohol abuse). Participants will be closely monitored during every study visit, and study treatment will be stopped if creatinine clearance decreases to <30 mL/min, or in case of alcohol abuse, circulatory dysfunction, or tissue hypoxia (e.g., acute heart failure). In case of general anesthesia, respiratory acidosis, severe dehydration, or use of iodinated contrast agents, study treatment will be temporarily discontinued. There is no evidence or scientific rationale as to why Galantamine would increase the risk of MALA.
Risks associated with Galantamine include a slow heart rate (bradycardia) and an increase in the time it takes for the heart's electrical system to recharge (QT-prolongation), particularly if the medication is overdosed. To limit these risks, participants will be monitored using ECG (recording of the heart's electrical signals), with participants excluded if they show significant QT prolongation or significant heart conduction problems. Participants will also begin by taking a lower dose of Galantamine (within RJx-01), which will be increased after 1-week (up-titration) if deemed safe to do so, up to a maximum dose of 12 mg/day. The use of Galantamine and similar medications in COPD patients with dementia didn't seem to pose any extra risks in a previous large study (Stephenson et al, 2012).
In our study, many COPD patients will be taking inhaled medications that work via similar pathways in the body to Galantamine, but these inhalers primarily target receptors in the lungs, while Galantamine works mostly in the brain, so they don't interfere much with how Galantamine works.
For RJx-01, the risk of GI side effects will be mitigated by administering study treatment during a meal.
Beyond standard of care the participants will undergo additional blood tests, breathing tests, and an oral IMP. These are all common routine tests. The blood and sputum sampling has minimal risk and mild discomfort. We will also monitor and analyse all potential cases of anaphylaxis and major adverse cardiac events (MACE). Several physical performance measures will be conducted in this trial by a trained Exercise Physiologist, Research Doctor, or Research Nurse. Procedures for these tests will be outlined in departmental standard operating procedure (SOP) documentation, which will be reviewed by all members of the study team.

For the optional skeletal muscle biopsy (sub-study) the skin is numbed using local anaesthetic and a small incision (less than 1 cm) is made. It is usual to experience some soreness for 24 – 48 hours after the procedure. The incision shall leave a small scar of less than 1 cm in length. There may also be some bruising around the site of the biopsy, called a haematoma. This will be performed by a qualified physician with experience conducting this procedure.

Where is the study run from?
NIHR Leicester Biomedical Research Centre (UK)

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

Who is funding the study?
Wellcome Leap (UK)

Who is the main contact?
1. Dr Neil Greening, neil.greening@leicester.ac.uk
2. Jill Clanchy, mint-copd@leicester.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Neil Greening

Contact details
NIHR Leicester Biomedical Research Centre – Respiratory
University Hospitals of Leicester NHS Trust
Glenfield Hospital
Leicester
United Kingdom
LE3 9QP
+44 (0)116 258 3663
neil.greening@leicester.ac.uk

Type(s)
Public

Contact name
Mrs Jill Clanchy

Contact details
NIHR Leicester Biomedical Research Centre – Respiratory
University Hospitals of Leicester NHS Trust
Glenfield Hospital
Leicester
United Kingdom

LE3 9QP
+44 (0)116 258 3370
mint-copd@leicester.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010818

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
1043

Central Portfolio Management System (CPMS)
64399

Study information

Scientific Title
A Phase IIa randomised, double-blind, placebo-controlled trial of RJx-01 to maintain the integrity of muscle during hospitalisation in older persons with severe acute exacerbation of chronic obstructive pulmonary disease

Acronym
MINT-COPD

Study objectives
Primary objective:
To evaluate the safety and tolerability of RJx-01 compared with placebo, between day 1 and day 197 following hospitalisation with an exacerbation of COPD (AECOPD).

Exploratory objectives:
To establish the effect of RJx-01 on muscle function, strength, mass, fatigability, and cellular and molecular dynamics, as well as exploratory safety, tolerability, and pharmacokinetics. Additionally, the study will assess its impact on frailty status, physical activity, health-related quality of life, fatigue, cognition, mortality, and healthcare utilisation following hospitalisation with an AECOPD, compared with placebo

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 28/03/2025, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8066, +44 (0)207 104 8227, +44 (0)207 104 8284; leicestercentral.rec@hra.nhs.uk), ref: 25/EM/0032

Study design
Double-blind randomized placebo-controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

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

Interventions
Participants will be randomised using an online randomisation software to receive either IMP (RJx-01) or placebo once daily (OD) for 168 days (~6 months). Stratification criteria will be applied during randomisation and will include pre-admission clinical frailty score (CFS) score (≤4, >4) and sex (male/female). Dosing will begin during hospital admission. Details of dosage and dosing schedule are detailed below:

IMP:
The active IMP consists of minitablets containing both metformin (MET) and galantamine (GAL) as active ingredients.
Following 7 days of continuous treatment, the dose will be titrated from 320 mg MET/ 6 mg GAL per day (equivalent to 150 minitablets MET and 6 minitablets GAL per day) to 960 mg MET / 12 mg GAL per day (equivalent to 450 minitablets MET and 12 minitablets GAL per day).

Placebo:
The placebo consists of minitablets containing placebo MET and GAL, with 0 mg of drug substance.
The placebo minitablets are visually indistinguishable from the IMP and contain the equivalent number of minitablets for each phase of administration.

Participants will be followed up with safety and exploratory outcomes measured before discharge and on days 8, 29, 57, 85, 113, 141, 169, and 197 (safety follow-up), as well as during any subsequent hospital admission(s). Other than the intervention described, all other care will be standard medical care delivered by the relevant clinical team.

Updated 02/02/2026:
Participants will be followed up with safety and exploratory outcomes measured before discharge and on days 7, 29, 57, 85, 113, 141, 169, and 197 (safety follow-up), as well as during any subsequent hospital admission(s). Other than the intervention described, all other care will be standard medical care delivered by the relevant clinical team.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)

RJx-01 [metformin hydrochloride, galantamine hydrobromide]

Primary outcome(s)

Current primary outcome measures as of 25/09/2025:
1. Adverse events (AEs) of CTCAE grade ≥3 that are at least possibly related to IMP in view of the investigator, recorded using participant self-reporting and electronic medical records at baseline (Visit 1), day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit
2. Serious adverse events (SAEs) that are at least possibly related to IMP are recorded using electronic medical records and participant reports at baseline (Visit 1), day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit
3. Hospital admissions (all-cause and COPD-related) are recorded through electronic medical records and participant self-reports at baseline (Visit 1) and monitored continuously until follow-up at day 197 (Visit 9)
4. Mortality (all-cause and COPD-related) is recorded using electronic medical records and death certificates from baseline (Visit 1) through follow-up at day 197 (Visit 9)

Previous primary outcome measures:
1. Adverse events (AEs) of CTCAE grade ≥3 that are at least possibly related to IMP in view of the investigator, recorded using participant self-reporting and electronic medical records at baseline (Visit 1), day 8 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit
2. Serious adverse events (SAEs) that are at least possibly related to IMP are recorded using electronic medical records and participant reports at baseline (Visit 1), day 8 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit
3. Hospital admissions (all-cause and COPD-related) are recorded through electronic medical records and participant self-reports at baseline (Visit 1) and monitored continuously until follow-up at day 197 (Visit 9)
4. Mortality (all-cause and COPD-related) is recorded using electronic medical records and death certificates from baseline (Visit 1) through follow-up at day 197 (Visit 9)

Key secondary outcome(s))

Current secondary outcome measures as of 02/02/2026:
Exploratory outcome measures:
1. Treatment-emergent adverse events (TEAEs) are recorded using participant self-reporting and electronic medical records at all study visits from baseline (Visit 1) to follow-up at day 197 (Visit 9), as well as at each hospital readmission visit.
2. Treatment-emergent serious adverse events (TESAEs) are recorded using electronic medical records and participant reports at all study visits from baseline (Visit 1) to follow-up at day 197 (Visit 9), as well as at each hospital readmission visit.
3. Clinical assessments (heart rate, blood pressure, temperature) are recorded at baseline (Visit 1), day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
4. ECG changes (QTc) are measured using standard electrocardiography (ECG) at baseline (Visit 1), day 7 (Visit 2), day 169 (Visit 8), and at each hospital readmission visit where clinically indicated.
5. Blood biomarkers (LFTs, HbA1c, full blood count, urea and electrolytes) are measured at baseline (Visit 1), day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission

visit.
6. Short Physical Performance Battery (SPPB) total score (5 sit-to-stand, balance score, 4-metre gait speed) is measured at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
7. Individual components of the SPPB (5 sit-to-stand, balance score, 4-metre gait speed) are measured at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit. Force dynamics will also be assessed during the 5 sit-to-stand test using a force plate.
8. Quadriceps maximal voluntary contraction (QMVC) is measured using an isometric dynamometer at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit. Force dynamics will also be assessed during the QMVC procedure.
9. Handgrip strength (HGS) is measured using a hand dynamometer at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
10. Quadriceps fatigability is measured using an isokinetic fatigue protocol with repeated leg extensions at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), and day 169 (Visit 8), and at each hospital readmission visit. Force dynamics will also be assessed during the quadriceps fatigability procedure.
11. Handgrip fatigability is measured using a repeated maximal grip strength test across 10 consecutive repetitions at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
12. Body composition is measured using bioelectrical impedance analysis (BIA) at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
13. Skeletal muscle mass is measured using dual-energy X-ray absorptiometry (DXA) at baseline (Visit 1), day 85 (Visit 5), and day 169 (Visit 8).
14. Quadriceps muscle volume is measured using magnetic resonance imaging (MRI) at baseline (Visit 1) and day 85 (Visit 5).
15. Patient-reported quality of life is measured using the St George’s Respiratory Questionnaire for COPD (SGRQ-C) at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), and follow-up at day 197 (Visit 9).
16. Patient-reported sarcopenia-related quality of life is measured using the SarQoL questionnaire at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), and follow-up at day 197 (Visit 9).
17. Sarcopenia risk is measured using the SARC-F questionnaire at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
18. Cognitive function is measured using the Mini-Addenbrooke's Cognitive Examination (Mini-ACE) at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), and day 169 (Visit 8).
19. Frailty is assessed using the Clinical Frailty Scale (CFS) at baseline (Visit 1), day 113 (Visit 6), and follow-up at day 197 (Visit 9).
20. Frailty phenotype is measured using Fried’s Frailty Phenotype criteria (unintentional weight loss, exhaustion, physical activity level, slowness, and weakness) at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
21. Physical activity is measured using a wearable accelerometer (assessing daily step count, moderate-to-vigorous physical activity, and inactivity time) continuously for 7 days at baseline (Visit 1), 7 days from day 29 (Visit 3), 7 days from day 57 (Visit 4), 7 days from day 85 (Visit 5), and 7 days from day 169 (Visit 8).
22. Lung function is measured using spirometry (FEV1, FVC, FEV1/FVC) at day 57 (Visit 4), and day 169 (Visit 8).
23. IMP acceptability is assessed using participant-reported questionnaires on day 57 (Visit 4)

and day 169 (Visit 8).
24. Pharmacokinetics of IMP is assessed using blood samples at day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 113 (Visit 6), day 169 (Visit 8), and at each hospital readmission visit.
25. Time to next hospital readmission is measured as the number of days from discharge after the index hospitalisation to the first subsequent readmission, tracked continuously until follow-up at day 197 (Visit 9).
26. Total hospital days are measured as the cumulative number of days participants spend in the hospital for any reason during the study period, recorded continuously until follow-up at day 197 (Visit 9).
27. Healthcare utilisation is assessed through self-reported and electronic medical record data on outpatient visits, community healthcare contacts, and uptake to pulmonary rehabilitation, tracked continuously until follow-up at day 197 (Visit 9).

Exploratory outcomes (skeletal muscle sub-study):
1. Muscle protein synthesis is measured using stable isotope tracer (D_2O) incorporation into muscle biopsy samples at baseline (Visit 1), day 57 (Visit 4), and day 113 (Visit 6).
2. Muscle protein breakdown is measured using stable isotope tracer (D_3-3-methylhistidine) in blood and urine samples at baseline (Visit 1) and day 57 (Visit 4).
3. Muscle biopsy (vastus lateralis) is performed to assess transcriptomic and proteomic changes at baseline (Visit 1), day 57 (Visit 4), and day 113 (Visit 6).

Previous secondary outcome measures as of 25/09/2025:
Exploratory outcome measures:
1. Treatment-emergent adverse events (TEAEs) are recorded using participant self-reporting and electronic medical records at all study visits from baseline (Visit 1) to follow-up at day 197 (Visit 9), as well as at each hospital readmission visit.
2. Treatment-emergent serious adverse events (TESAEs) are recorded using electronic medical records and participant reports at all study visits from baseline (Visit 1) to follow-up at day 197 (Visit 9), as well as at each hospital readmission visit.
3. Clinical assessments (heart rate, blood pressure, temperature) are recorded at baseline (Visit 1), day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
4. ECG changes (QTc) are measured using standard electrocardiography (ECG) at baseline (Visit 1), day 7 (Visit 2), day 169 (Visit 8), and at each hospital readmission visit where clinically indicated.
5. Blood biomarkers (LFTs, HbA1c, full blood count, urea and electrolytes) are measured at baseline (Visit 1), day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
6. Short Physical Performance Battery (SPPB) total score (5 sit-to-stand, balance score, 4-metre gait speed) is measured at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
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8. Quadriceps maximal voluntary contraction (QMVC) is measured using an isometric dynamometer at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit. Force dynamics will also be assessed during the QMVC procedure.
9. Handgrip strength (HGS) is measured using a hand dynamometer at baseline (Visit 1), day 29

(Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
10. Quadriceps fatigability is measured using an isokinetic fatigue protocol with repeated leg extensions at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), and day 169 (Visit 8), and at each hospital readmission visit. Force dynamics will also be assessed during the quadriceps fatigability procedure.
11. Handgrip fatigability is measured using a repeated maximal grip strength test across 10 consecutive repetitions at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
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17. Sarcopenia risk is measured using the SARC-F questionnaire at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
18. Fatigue is measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
19. Cognitive function is measured using the Mini-Addenbrooke's Cognitive Examination (Mini-ACE) at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), and day 169 (Visit 8).
20. Frailty is assessed using the Clinical Frailty Scale (CFS) at baseline (Visit 1), day 113 (Visit 6), and follow-up at day 197 (Visit 9).
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24. IMP acceptability is assessed using participant-reported questionnaires on day 57 (Visit 4) and day 169 (Visit 8).
25. Pharmacokinetics of IMP is assessed using blood samples at day 7 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 113 (Visit 6), day 169 (Visit 8), and at each hospital readmission visit.
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tracked continuously until follow-up at day 197 (Visit 9).

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2. Muscle protein breakdown is measured using stable isotope tracer (D_3-3-methylhistidine) in blood and urine samples at baseline (Visit 1) and day 57 (Visit 4).
3. Muscle biopsy (vastus lateralis) is performed to assess transcriptomic and proteomic changes at baseline (Visit 1), day 57 (Visit 4), and day 113 (Visit 6).

Previous secondary outcome measures:
Exploratory outcome measures:
1. Treatment-emergent adverse events (TEAEs) are recorded using participant self-reporting and electronic medical records at all study visits from baseline (Visit 1) to follow-up at day 197 (Visit 9), as well as at each hospital readmission visit.
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4. ECG changes (QTc) are measured using standard electrocardiography (ECG) at baseline (Visit 1), day 8 (Visit 2), day 169 (Visit 8), and at each hospital readmission visit where clinically indicated.
5. Blood biomarkers (LFTs, HbA1c, full blood count, urea and electrolytes) are measured at baseline (Visit 1), day 8 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
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12. Body composition is measured using bioelectrical impedance analysis (BIA) at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169

(Visit 8), follow-up at day 197 (Visit 9), and at each hospital readmission visit.
13. Skeletal muscle mass is measured using dual-energy X-ray absorptiometry (DXA) at baseline (Visit 1), day 85 (Visit 5), and day 169 (Visit 8).
14. Quadriceps muscle volume is measured using magnetic resonance imaging (MRI) at baseline (Visit 1) and day 85 (Visit 5).
15. Patient-reported quality of life is measured using the St George's Respiratory Questionnaire for COPD (SGRQ-C) at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), and follow-up at day 197 (Visit 9).
16. Patient-reported sarcopenia-related quality of life is measured using the SarQoL questionnaire at baseline (Visit 1), day 29 (Visit 3), day 57 (Visit 4), day 85 (Visit 5), day 113 (Visit 6), day 141 (Visit 7), day 169 (Visit 8), and follow-up at day 197 (Visit 9).
17. Sarcopenia risk is measured using the SARC-F questionnaire at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
18. Fatigue is measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
19. Cognitive function is measured using the Mini-Addenbrooke's Cognitive Examination (Mini-ACE) at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), and day 169 (Visit 8).
20. Frailty is assessed using the Clinical Frailty Scale (CFS) at baseline (Visit 1), day 113 (Visit 6), and follow-up at day 197 (Visit 9).
21. Frailty phenotype is measured using Fried's Frailty Phenotype criteria (unintentional weight loss, exhaustion, physical activity level, slowness, and weakness) at baseline (Visit 1), day 29 (Visit 3), day 85 (Visit 5), day 169 (Visit 8), and at each hospital readmission visit.
22. Physical activity is measured using a wearable accelerometer (assessing daily step count, moderate-to-vigorous physical activity, and inactivity time) continuously for 7 days at baseline (Visit 1), 14 days from day 29 (Visit 3), 14 days from day 57 (Visit 4), 14 days from day 85 (Visit 5), and 14 days from day 169 (Visit 8).
23. Lung function is measured using spirometry (FEV1, FVC, FEV1/FVC) at day 57 (Visit 4), and day 169 (Visit 8).
24. IMP acceptability is assessed using participant-reported questionnaires on day 57 (Visit 4) and day 169 (Visit 8).
25. Pharmacokinetics of IMP is assessed using blood samples at day 8 (Visit 2), day 29 (Visit 3), day 57 (Visit 4), day 113 (Visit 6), day 169 (Visit 8), and at each hospital readmission visit.
26. Time to next hospital readmission is measured as the number of days from discharge after the index hospitalisation to the first subsequent readmission, tracked continuously until follow-up at day 197 (Visit 9).
27. Total hospital days are measured as the cumulative number of days participants spend in the hospital for any reason during the study period, recorded continuously until follow-up at day 197 (Visit 9).
28. Healthcare utilisation is assessed through self-reported and electronic medical record data on outpatient visits, community healthcare contacts, and uptake to pulmonary rehabilitation, tracked continuously until follow-up at day 197 (Visit 9).

Exploratory outcomes (skeletal muscle sub-study):
1. Muscle protein synthesis is measured using stable isotope tracer (D_2O) incorporation into muscle biopsy samples at baseline (Visit 1), day 57 (Visit 4), and day 113 (Visit 6).
2. Muscle protein breakdown is measured using stable isotope tracer (D_3-3-methylhistidine) in blood and urine samples at baseline (Visit 1) and day 57 (Visit 4).
3. Muscle biopsy (vastus lateralis) is performed to assess transcriptomic and proteomic changes at baseline (Visit 1), day 57 (Visit 4), and day 113 (Visit 6).

Completion date

31/08/2028

Eligibility

Key inclusion criteria

Current inclusion criteria as of 02/02/2026:
1. Symptoms typical of COPD when stable, defined as all of:
1.1. Baseline extended MRC dyspnoea grade ≥3 when stable
1.2. FEV1/FVC ratio <0.7 (only if previous spirometry available)
1.3. Usually on maintenance inhaled therapy for COPD (any of long-acting muscarinic antagonist [LAMA], Long-acting beta-agonist [LABA] +/- Inhaled Corticosteroid [ICS])
2. A clinician defined acute exacerbation of COPD (AECOPD) requiring admission to hospital and change in treatment (e.g. addition of systemic corticosteroids +/- antibiotics)
3. Able to initiate the first dose of the IMP when medically fit for discharge from hospital
4. Current or ex-smoker with cumulative smoking history ≥10 pack years
5. Age ≥45 years at time of screening
6. Predicted length of hospital stay ≥48 hours
7. Willing and able to consent to participate in the trial
8. Able to understand written and spoken English to a level so able to complete study measures, or with support from English-speaking family
9. If male with a partner who is a woman of childbearing potential (WOCBP), then willingness to comply with protocol contraception requirements (section 10.9)

Sub-study inclusion criteria
1. Meets eligibility criteria and has consented to participate in the COPD-MINT main trial
2. Willing and able to consent to participate in the sub-study

Previous inclusion criteria:
1. Symptoms typical of COPD when stable, defined as all of:
1.1. Baseline extended MRC dyspnoea grade ≥3 when stable
1.2. FEV1/FVC ratio <0.7 (only if previous spirometry available)
1.3. Usually on maintenance inhaled therapy for COPD (any of long-acting muscarinic antagonist [LAMA], Long-acting beta-agonist [LABA] +/- Inhaled Corticosteroid [ICS])
2. A clinician defined acute exacerbation of COPD (AECOPD) requiring admission to hospital and change in treatment (e.g. addition of systemic corticosteroids +/- antibiotics)
3. Able to initiate the first dose of the IMP when medically fit for discharge from hospital
4. Current or ex-smoker with cumulative smoking history ≥10 pack years
5. Age ≥55 years at time of screening
6. Predicted length of hospital stay ≥48 hours
7. Willing and able to consent to participate in the trial
8. Able to understand written and spoken English to a level so able to complete study measures, or with support from English-speaking family
9. If male with a partner who is a woman of childbearing potential (WOCBP), then willingness to comply with protocol contraception requirements (section 10.9)

Sub-study inclusion criteria
1. Meets eligibility criteria and has consented to participate in the COPD-MINT main trial
2. Willing and able to consent to participate in the sub-study

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
45 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 02/02/2026:
1. Use of, or contraindication to, metformin , any acetylcholinesterase inhibitor (AChE-I) medication (including Galantamine), or any systemic medication with significant cholinergic or anticholinergic effects within 6 months prior to screening or during the study period, except for long-acting muscarinic antagonist (LAMA) inhalers.
2. Patients with known hypersensitivity to MET, GAL or any excipients used in the formulations, including tartrazine (FD&C yellow number 5)
3. Hospital admission within the 2 weeks prior to the first day of current hospital admission.
4. ≥3 emergency/unplanned hospital admissions in the previous 6 months.
5. Unstable or life-threatening cardiac disease, including myocardial infarction or unstable angina in the previous 12 months (added 02/07/2025: excluding Type 2 myocardial infarction).
6. Unstable or life-threatening cardiac arrhythmia requiring intervention in the previous 3 months, QTc >500 msec or 2nd or 3rd degree Bundle Branch block, or subjects who are at increased risk of QTc prolongation in the view of the investigator including due to concurrent use of multiple medications known to increase the risk of QTc prolongation.
7. Clinical evidence of congestive cardiac failure as the primary cause of dyspnoea or physical limitation.
8. Normally bed-bound (Clinical Frailty Score 8 or higher).
9. Women of childbearing potential (WOCBP) or those who are currently pregnant or breastfeeding
10. Patients whose treatment is considered palliative due to a condition other than COPD (life expectancy <3 months).
11. Anticipated prolonged delay to hospital discharge due to social (non-medical) issues.
12. Other conditions including current known active cancer, interstitial lung disease, primary pulmonary hypertension, significant circulatory dysfunction (e.g., acute heart failure, sepsis, shock, severe dehydration), chronic liver disease, active drug and/or alcohol abuse or any other conditions that in the view of the investigator will affect the trial.
13. Participation in an interventional clinical trial within 3 months of screening or receipt of any investigational medicinal product within 3 months or 5 half-lives.
14. Evidence of hepatic insufficiency, defined as ALT or AST levels greater than 3 times the upper limit of normal.

15. Severe Renal Impairment with CrCl <30 ml/min (by Cockcroft-Gault Equation).
16. Concomitant or recent treatment with any prescription drug (<3 months) or nonprescription treatment (<2 weeks) known to affect muscle mass (e.g., with anabolic or catabolic effects), including testosterone replacement treatment, anti-androgens (such as LHRH agonists), anti-oestrogens (tamoxifen, etc.), recombinant growth hormone, Megestrol, etc.
17. Participants taking >20 mg/day oral prednisolone (or equivalent systemic corticosteroid dose) consistently for >28 days immediately prior to screening.
18. Concomitant or recent treatment (<3 months) with an immunosuppressant agent (e.g. Disease-modifying antirheumatic drugs or monoclonal antibodies, with the exception of corticosteroids).

Sub-study exclusion criteria:
1. Impaired blood clotting (family or medical history of impaired blood clotting, e.g., haemophilia)
2. Current use of warfarin, therapeutic doses of low molecular weight heparin or any direct oral anticoagulant (DOAC) drugs (including but not limited to betrixaban, apixaban, edoxaban, rivaroxaban, dabigatran)
3. Current use of antiplatelet agents (other than aspirin at a dose <75 mg/day)

Previous exclusion criteria as of 25/09/2025:
1. Use of any antidiabetic medication (including Metformin), any acetylcholinesterase inhibitor (AChE-I) medication (including Galantamine), or any systemic medication with significant cholinergic or anticholinergic effects within 6 months prior to screening or during the study period, except for long-acting muscarinic antagonist (LAMA) inhalers.
2. Patients with known hypersensitivity to MET, GAL or any excipients used in the formulations, including tartrazine (FD&C yellow number 5)
3. Hospital admission within the 2 weeks prior to the first day of current hospital admission.
4. ≥3 emergency/unplanned hospital admissions in the previous 6 months.
5. Unstable or life-threatening cardiac disease, including myocardial infarction or unstable angina in the previous 12 months (added 02/07/2025: excluding Type 2 myocardial infarction).
6. Unstable or life-threatening cardiac arrhythmia requiring intervention in the previous 3 months, QTc >500 msec or 2nd or 3rd degree Bundle Branch block, or subjects who are at increased risk of QTc prolongation in the view of the investigator including due to concurrent use of multiple medications known to increase the risk of QTc prolongation.
7. Clinical evidence of congestive cardiac failure as the primary cause of dyspnoea or physical limitation.
8. Normally bed-bound (Clinical Frailty Score 8 or higher).
9. Women of childbearing potential (WOCBP) or those who are currently pregnant or breastfeeding
10. Patients whose treatment is considered palliative due to a condition other than COPD (life expectancy <3 months).
11. Anticipated prolonged delay to hospital discharge due to social (non-medical) issues.
12. Other conditions including current diabetes mellitus, active cancer, interstitial lung disease, primary pulmonary hypertension, significant circulatory dysfunction (e.g., acute heart failure, sepsis, shock, severe dehydration), chronic liver disease, drug and/or alcohol abuse or any other conditions that in the view of the investigator will affect the trial.
13. Participation in an interventional clinical trial within 3 months of screening or receipt of any investigational medicinal product within 3 months or 5 half-lives.
14. Evidence of hepatic insufficiency, defined as ALT or AST levels greater than 3 times the upper limit of normal.
15. Severe Renal Impairment with CrCl <30 ml/min (by Cockcroft-Gault Equation).
16. Concomitant or recent treatment with any prescription drug (<3 months) or nonprescription treatment (<2 weeks) known to affect muscle mass (e.g., with anabolic or catabolic effects),

including testosterone replacement treatment, anti-androgens (such as LHRH agonists), anti-oestrogens (tamoxifen, etc.), recombinant growth hormone, Megestrol, etc.
17. Participants taking >20 mg/day oral prednisolone (or equivalent systemic corticosteroid dose) consistently for >28 days prior to screening.
18. Concomitant or recent treatment (<3 months) with an immunosuppressant agent (e.g. Disease-modifying antirheumatic drugs or monoclonal antibodies, with the exception of corticosteroids).

Sub-study exclusion criteria:
1. Impaired blood clotting (family or medical history of impaired blood clotting, e.g., haemophilia)
2. Current use of warfarin, therapeutic doses of low molecular weight heparin* or any direct oral anti-coagulant (DOAC) drugs (including but not limited to betrixaban, apixaban, edoxaban, rivaroxaban, dabigatran)
3. Current use of antiplatelet agents (other than aspirin at a dose <75 mg/day)

* Defined as enoxaparin >40 mg / day; tinzaparin >50 IU / kg / day; dalteparin sodium >5000 IU / day

Previous exclusion criteria:
1. Use of any antidiabetic medication (including Metformin), any acetylcholinesterase inhibitor (AChE-I) medication (including Galantamine), or any systemic medication with significant cholinergic or anticholinergic effects within 6 months prior to screening or during the study period, except for long-acting muscarinic antagonist (LAMA) inhalers.
2. Patients with known hypersensitivity to MET, GAL or any excipients used in the formulations, including tartrazine (FD&C yellow number 5)
3. Hospital admission within the 4 weeks prior to the first day of current hospital admission.
4. ≥4 emergency/unplanned hospital admissions in the previous 12 months.
5. Unstable or life-threatening cardiac disease, including myocardial infarction or unstable angina in the previous 12 months (added 02/07/2025: excluding Type 2 myocardial infarction).
6. Unstable or life-threatening cardiac arrhythmia requiring intervention in the previous 3 months, QTc >500 msec or 2nd or 3rd degree Bundle Branch block.
7. Clinical evidence of congestive cardiac failure as the primary cause of dyspnoea or physical limitation.
8. Normally bed-bound (Clinical Frailty Score 8 or higher).
9. Women of childbearing potential (WOCBP) or those who are currently pregnant or breastfeeding
10. Patients whose treatment is considered palliative due to a condition other than COPD (life expectancy <3 months).
11. Anticipated prolonged delay to hospital discharge due to social (non-medical) issues.
12. Other conditions including current diabetes mellitus, active cancer, interstitial lung disease, primary pulmonary hypertension, significant circulatory dysfunction (e.g., acute heart failure, sepsis, shock, severe dehydration), chronic liver disease, drug and/or alcohol abuse or any other conditions that in the view of the investigator will affect the trial.
13. Participation in an interventional clinical trial within 3 months of screening or receipt of any investigational medicinal product within 3 months or 5 half-lives.
14. Evidence of hepatic insufficiency, defined as ALT or AST levels greater than 3 times the upper limit of normal.
15. Severe Renal Impairment with CrCl <30 ml/min (by Cockcroft-Gault Equation).
16. Concomitant or recent treatment with any prescription drug (<3 months) or nonprescription treatment (<2 weeks) known to affect muscle mass (e.g., with anabolic or catabolic effects), including testosterone replacement treatment, anti-androgens (such as LHRH agonists), anti-oestrogens (tamoxifen, etc.), recombinant growth hormone, Megestrol, etc.

17. Participants taking >20 mg/day oral prednisolone (or equivalent systemic corticosteroid dose) consistently for >28 days prior to screening.
18. Concomitant or recent treatment (<3 months) with an immunosuppressant agent (e.g. Disease-modifying antirheumatic drugs or monoclonal antibodies, with the exception of corticosteroids).

Sub-study exclusion criteria:
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2. Current use of warfarin, therapeutic doses of low molecular weight heparin* or any direct oral anti-coagulant (DOAC) drugs (including but not limited to betrixaban, apixaban, edoxaban, rivaroxaban, dabigatran)
3. Current use of antiplatelet agents (other than aspirin at a dose <75 mg/day)

* Defined as enoxaparin >40 mg / day; tinzaparin >50 IU / kg / day; dalteparin sodium >5000 IU / day

Date of first enrolment
12/05/2025

Date of final enrolment
30/11/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals of Leicester NHS Trust
Glenfield Hospital
Groby Road
Leicester
England
LE3 9QP

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Charity

Funder Name
Wellcome Leap

Alternative Name(s)
Leap, Wellcome Leap Inc, Wellcome Leap, Inc.

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes