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Using advanced MRI scans and muscle function tests to study muscle changes in adults with Pompe disease receiving enzyme replacement therapy

Submission date
12/06/2026

Recruitment status
Not yet recruiting

Registration date
15/06/2026

Overall study status
Ongoing

Last Edited
12/06/2026

Condition category
Nutritional, Metabolic, Endocrine

[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
Pompe disease is a rare genetic condition that causes glycogen, a stored form of sugar, to build up inside muscle cells. Over time, this can damage muscles and lead to muscle weakness, problems with movement, and breathing difficulties.
The PRISM study aims to find out whether advanced MRI scans can measure changes in muscle structure and muscle glycogen in adults with late-onset Pompe disease (LOPD). The study will also look at how these MRI findings relate to muscle strength, physical function, walking, breathing tests, and blood and urine markers.
Participants with late-onset Pompe disease are already receiving enzyme replacement therapy as part of their usual NHS care. The study does not change, assign, stop, or compare treatments. Treatment decisions remain entirely between participants and their clinical team.

Who can participate?
Adults aged 18 years or over may be able to take part.
The study will include adults with late-onset Pompe disease who are already receiving enzyme replacement therapy (ERT) as part of routine clinical care.
The study will also include healthy adult volunteers without Pompe disease. Healthy volunteers will be matched by age and sex to participants with Pompe disease and will help the researchers understand what normal muscle measurements look like.
People cannot take part if they are unable to have an MRI scan, are pregnant, cannot lie flat for the scan, cannot give informed consent, or if the study team considers that taking part would not be suitable for them.

What does the study involve?
Participants with LOPD will attend study visits in Newcastle upon Tyne over two years. These visits will take place at the start of the study, after 1 year, and after 2 years.
Healthy volunteers will attend one study visit only.
Study visits may include:

1. MRI scans of the thigh muscles, including a specialised carbon-13 scan to measure muscle glycogen
2. Muscle strength and physical function tests
3. Walking and gait analysis tests
4. Breathing tests
5. Questionnaires about health and daily activities
6. Blood and urine sample collection
7. Review of relevant medical history and current medication

Three of the 30 participants with LOPD will also be invited to take part in an additional sub-study at the start of PRISM. This involves extra MRI scans around one of their routine enzyme replacement therapy infusions. This will help the researchers understand whether the timing of the scan in relation to routine treatment affects muscle glycogen measurements.
Taking part in the study is voluntary. Participants can decide not to take part or withdraw later without giving a reason. This will not affect their usual medical care.

What are the possible benefits and risks of participating?
Participants may not receive a direct personal benefit from taking part. The information collected may help researchers better understand how to measure muscle changes in Pompe disease and may support better monitoring methods in the future.
The MRI scan does not use radiation. Some people may find the scan uncomfortable because they need to lie still, and the scanner can be noisy. Some people may feel anxious or claustrophobic. The research team will explain the scan beforehand, and participants can speak to the team during the scan.
Blood sampling may cause brief discomfort, bruising, bleeding, or, rarely, infection. Physical tests and walking assessments may cause tiredness or muscle discomfort. The study team will monitor participants during assessments, and breaks will be provided when needed.
Personal information and study data will be handled securely and confidentially in line with data protection requirements.

Where is the study run from?
The study is run from the John Walton Muscular Dystrophy Research Centre at Newcastle University and the Newcastle upon Tyne Hospitals NHS Foundation Trust (UK).
MRI scans will take place at the Newcastle Magnetic Resonance Centre, Newcastle upon Tyne.
Physical assessments and sample collection will take place at the Clinical Research Facility at the Royal Victoria Infirmary, Newcastle upon Tyne.

When is the study starting and how long is it expected to run for?
July 2026 to December 2029

Who is funding the study?
Amicus Therapeutics (USA)

Who is the main contact?
Prof. Jordi Diaz-Manera, jordi.diaz-manera@newcastle.ac.uk

Contact information

Type(s)
Principal investigator

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Integrated Research Application System (IRAS)
370049

R&D
11186

Study information

Scientific Title
PRISM: a single-centre prospective longitudinal observational cohort study of patients with Pompe disease treated with enzyme replacement therapy using muscle MRI and muscle function tests

Acronym
PRISM

Study objectives
PRISM is taking place because late-onset Pompe disease causes glycogen accumulation in skeletal muscle, leading to progressive muscle damage, weakness, functional decline and respiratory involvement. Although enzyme replacement therapy (ERT) is part of routine clinical care for eligible patients, there remains a need for better non-invasive methods to measure muscle glycogen, muscle structure and disease progression over time.

The research question, or main objective, of this observational study is to assess whether muscle MRI and carbon-13 magnetic resonance spectroscopy can identify and quantify changes in muscle structure and muscle glycogen content in adults with late-onset Pompe disease who are already receiving licensed ERT as part of routine clinical care and correlate these changes with muscle function.

The study objectives are:
1. To study changes in thigh muscle fat fraction over 2 years using three-point Dixon MRI.
2. To study changes in thigh muscle T2 relaxation time over 2 years.
3. To identify and quantify glycogen content in the muscles of the left lower limb using carbon-13 magnetic resonance spectroscopy and assess whether it changes over 2 years.
4. To collect demographic information and disease history data from participants with late-onset Pompe disease and assess how these relate to structural changes observed using MRI.
5. To study changes in skeletal and respiratory muscle function over 2 years using a battery of muscle function tests.
6. To collect blood and urine samples from participants for storage in the John Walton Muscular Dystrophy Research Centre (JWMDRC) Biobank for future research.

A small pivotal sub-study will assess whether the timing of carbon-13 magnetic resonance spectroscopy in relation to routine fortnightly enzyme replacement therapy infusion influences muscle glycogen measurements. This will help determine the most appropriate timing for subsequent spectroscopy assessments in the longitudinal phase.

The study does not administer, assign, modify or compare treatments. All treatment decisions remain part of routine clinical care and are not influenced by participation in PRISM.

Ethics approval required
Ethics approval required

Ethics approval(s)
submitted 02/06/2026, West Midlands - South Birmingham Research Ethics Committee (2 Redman Place Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8121; southbirmingham.rec@hra.nhs.uk), ref: 26/WM/0118

Primary study design
Observational

Secondary study design
Cohort study

Study type(s)

Health condition(s) or problem(s) studied
Pompe disease

Interventions
PRISM is a single-centre, prospective, longitudinal, observational cohort study conducted in the JWMDRC, in Newcastle upon Tyne, UK.

The study recruits 40 adult participants: 30 adults with late-onset Pompe disease (LOPD) who are already receiving licensed enzyme replacement therapy (ERT) as part of routine clinical care, and 10 age- and sex-matched healthy controls. Participants with late-onset Pompe disease are observed in two cohorts according to the licensed ERT they are already receiving in routine care: cipaglucosidase alfa plus miglustat or avalglucosidase alfa. The study does not administer, assign, modify or compare treatment.

A small pivotal sub-study is conducted before the main longitudinal phase. Three of the 30 participants with LOPD disease receiving routine fortnightly ERT undergo carbon-13 magnetic resonance spectroscopy at three timepoints within a single infusion cycle: Day-1 after infusion, Day-7 after infusion, and Day-14 after infusion. This assesses whether the timing of spectroscopy in relation to routine enzyme replacement therapy infusion influences muscle glycogen measurements and informs the timing of subsequent spectroscopy assessments in the longitudinal phase.

Participants with LOPD attend study assessments at baseline, Year 1 and Year 2. Healthy controls attend a single baseline visit only. At each relevant visit, participants undergo muscle MRI and carbon-13 magnetic resonance spectroscopy to assess thigh muscle structure, fat fraction, muscle water T2 relaxation time and muscle glycogen content in the left lower limb.

Clinical and functional assessments include demographic and disease history data collection, medical history, concomitant medication review, adverse event and serious adverse event review, patient-reported outcome measures, the 100-metre timed test, the 10-metre walk-carrying test, Timed Up and Go, the North Star Assessment for Limb-Girdle Type Muscular Dystrophies, Performance of Upper Limb entry item, the Biering-Sorenson back extensor test, handheld dynamometry, pulmonary function testing, and gait analysis using the 6-minute walk test.

Blood and urine samples are collected from participants for storage in the JWMDRC Biobank for future research, subject to consent.

Intervention Type
Other

Primary outcome(s)
1. MRI-derived thigh muscle structure and composition measured using fat fraction, cross-sectional area, contractile cross-sectional area and muscle water T2 relaxation time of the thigh muscles measured using 3-point Dixon MRI and muscle water T2 MRI, at baseline, Year 1 and Year 2 for participants with late-onset Pompe disease, and baseline only for healthy controls

2. Muscle glycogen content in the muscles of the left lower limb measured using carbon-13 magnetic resonance spectroscopy at baseline, Year 1 and Year 2 for participants with late-onset Pompe disease, and baseline only for healthy controls

3. Pivotal sub-study: short-term variation in thigh muscle glycogen content across the routine enzyme replacement therapy infusion cycle measured using carbon-13 magnetic resonance spectroscopy in a subset of three participants with late-onset Pompe disease at Day 1 after routine enzyme replacement therapy infusion, Day 7 after infusion, and Day 14 after infusion

Key secondary outcome(s))
1. Skeletal muscle functional outcomes measured using standardised functional assessments, including RPACT, 100-metre timed test, 10-metre walk-carrying test, Timed Up and Go, North Star Assessment for Limb-Girdle Type Muscular Dystrophies, Performance of Upper Limb entry item, Biering-Sorenson back extensor test, handheld dynamometry, 6-minute walk test, and gait analysis at baseline, Year 1 and Year 2 for participants with late-onset Pompe disease, and baseline only for healthy controls

2. Pulmonary function outcomes measured using spirometric and respiratory pressure measures, including seated forced vital capacity, supine forced vital capacity, maximal inspiratory pressure and maximal expiratory pressure, at baseline, Year 1 and Year 2 for participants with late-onset Pompe disease, and baseline only for healthy controls

3. Biomarkers measured using blood and urine samples collected and stored in the JWMDRC Biobank for future research, where authorised by participant consent, at baseline, Year 1 and Year 2 for participants with late-onset Pompe disease, and baseline only for healthy controls

Completion date
31/12/2029

Eligibility

Key inclusion criteria
1. Adults aged 18 years or over
2. Able and willing to provide informed consent
3. Ambulatory, able to walk with or without assistive devices
4. No contraindications to MRI
5. Able and willing to complete the relevant study assessments, including MRI and carbon-13 magnetic resonance spectroscopy, muscle function tests, pulmonary function tests where applicable, gait analysis, questionnaires, wearable monitoring where applicable, and blood and urine sample collection
6. For participants with late-onset Pompe disease:
6.1. Confirmed diagnosis of late-onset Pompe disease, based on recommendations recently proposed by the European Pompe Consortium: reduced enzymatic activity in leukocytes, fibroblasts or skeletal muscle and/or by the presence of two mutations in the GAA gene
6.2. Symptoms started after 2 years of age and are compatible with a clinical diagnosis of late-onset Pompe disease
6.3. Receiving licensed enzyme replacement therapy (ERT) as part of routine clinical care (either cipaglucosidase alfa plus miglustat or avalglucosidase alfa)
6.4. Medical Research Council quadriceps muscle score of 3 or above
7. For healthy controls: adults without Pompe disease who are age- and sex-matched to participants with late-onset Pompe disease.

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 years

Upper age limit
120 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Contraindications for MRI such as having a metallic prosthesis, pacemaker or any other device that makes the completion of an MRI impossible
2. Having claustrophobia or other conditions that could limit the capacity of the patient to be located inside the MRI
3. Inability to lie supine for up to 60 min
4. Unwillingness to complete all study-related activity
5. Pregnancy, for female participants of childbearing potential
6. Inability to understand the study information or provide informed consent
7. Any other reason which, in the opinion of the study team, makes participation unsuitable

Date of first enrolment
01/07/2026

Date of final enrolment
31/12/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The John Walton Muscular Dystrophy Research Centre
Institute of Genetic Medicine
International Centre for Life
Newcastle University
Newcastle upon Tyne
England
NE1 3BZ

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
England
NE7 7DN

Study participating centre
Newcastle Magnetic Resonance Centre
Campus for Ageing and Vitality
Newcastle University
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NE4 5PL

Study participating centre
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Level 6 Leazes Wing
Royal Victoria Infirmary
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Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type

Funder Name

Amicus Therapeutics

Alternative Name(s)
Amicus Therapeutics, Inc., Amicus

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available