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# Carbon spectroscopy MRI: a non-invasive tool to detect late-onset Pompe disease (LOPD)

**Submission date**
15/06/2022

**Recruitment status**
Recruiting

**Registration date**
07/07/2022

**Overall study status**
Ongoing

**Last Edited**
11/06/2026

**Condition category**
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[X] 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 caused by changes in the GAA gene. These changes mean that the body does not produce enough of an enzyme called acid alpha-glucosidase. This enzyme normally helps break down glycogen, which is a stored form of sugar. In people with Pompe disease, glycogen can build up inside the muscles and other tissues.
Late-onset Pompe disease (LOPD) usually develops later in childhood or adulthood. It can cause progressive muscle weakness, walking difficulties, breathing problems and, in some people, the need for ventilation support.
Enzyme replacement therapy (ERT) is available for Pompe disease and can help stabilise or improve muscle and breathing function. However, there is currently no reliable non-invasive test to measure glycogen build-up in skeletal muscle. At present, measuring glycogen directly usually requires a muscle biopsy, which is invasive.
This study aims to investigate whether carbon-13 magnetic resonance spectroscopy (13C-MR spectroscopy), a specialist MRI technique, can identify and measure glycogen in the skeletal muscles of people with Pompe disease. The study will also assess whether MRI findings relate to muscle function and whether this technique could help monitor disease progression and response to treatment.

Who can participate?
This study includes two recruitment phases.
The original recruitment phase is now completed. It included:
1. Ten (10) people with Pompe disease in the early stages of disease progression.
2. Ten (10) healthy volunteers matched by age and sex with those 10 people with Pompe disease.

The current extension phase is recruiting:
1. Five (5) additional people with LOPD who are at a middle stage of disease progression and are already receiving ERT.
People taking part must be aged 12 years or older, have no contraindications to MRI, and be willing to complete the study assessments.
Healthy volunteers are not being recruited during the current extension phase.

What does the study involve?
This is an observational study. This means that participants do not receive a study treatment as part of the research and are not randomised into different groups.
In the original recruitment phase, people with Pompe disease attended two study visits: one at the start of the study and one after 12 months. Healthy volunteers attended one baseline visit only.
In the current extension phase, 5 people with LOPD will attend a baseline visit and a year 1 visit. These visits include clinical assessment, muscle function tests, patient-reported questionnaires, blood and urine sample collection, and MRI scans of the legs.
Muscle function tests measure strength and physical performance, such as walking, standing up from a chair, squatting, and other movements that can be affected by Pompe disease.
Of the 5 participants in the current extension phase, 3 will also attend an additional MRI visit 5 to 7 days after one of their usual ERT infusions. This will help the researchers explore whether muscle glycogen changes after treatment.
The MRI scans include carbon-13 magnetic resonance spectroscopy (13C-MR spectroscopy), which is used to measure glycogen in muscle. The MRI scans also measure muscle water and fat.
Some participants will also have additional MRI measurements using a new, larger 12 cm carbon coil. This will be compared with the previous 6 cm coil to assess whether it improves glycogen measurement in deeper muscles.
Blood and urine samples may be stored for future research into biomarkers related to Pompe disease, disease progression and muscle MRI findings.

What are the possible benefits and risks of participating?
Participants are not expected to benefit directly from taking part in this study. However, the information collected may help researchers understand whether MRI can be used to measure glycogen in muscle and monitor Pompe disease in the future.
MRI scanning does not use ionising radiation and is considered safe for repeated use. Some people may find the scanner noisy or uncomfortable or may feel claustrophobic. The MRI scan can be stopped if needed.
Blood collection may cause brief discomfort, bruising, bleeding, fainting, or a very small risk of infection where the needle enters the skin. Urine collection does not pose a significant risk.
Muscle function tests do not usually pose significant risks, although participants may feel tired or there may be a small risk of falling during walking or movement tests.
Travel and meal expenses will be reimbursed for the participant and one accompanying person, where applicable.

Where is the study run from?
The study is run from Newcastle upon Tyne Hospitals NHS Foundation Trust, UK, in collaboration with Newcastle University. Study visits take place at the Newcastle Magnetic Resonance Centre and the NIHR Newcastle Clinical Research Facility at the Royal Victoria Infirmary.

When is the study starting and how long is it expected to run for?
The study started in January 2022 and is expected to run until December 2028.

Who is funding the study?
Sanofi (France)

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

# Contact information

**Type(s)**
Principal investigator, Scientific

**Contact name**
Prof Jordi Diaz Manera

**ORCID ID**
https://orcid.org/0000-0003-2941-7988

**Contact details**
The John Walton Muscular Dystrophy Research Centre
Translational and Clinical Research Institute
Newcastle University
International Centre for Life
Newcastle upon Tyne
United Kingdom
NE1 3BZ
+44 (0)1912418602
jordi.diaz-manera@newcastle.ac.uk

**Type(s)**
Public

**Contact name**
Mr Alejandro Gonzalez Chamorro

**ORCID ID**
https://orcid.org/0009-0001-7067-0216

**Contact details**
The John Walton Muscular Dystrophy Research Centre
Translational and Clinical Research Institute
Newcastle University
International Centre for Life
Newcastle upon Tyne
United Kingdom
NE1 3BZ
+44 (0)191 241 8652
alejandro.gonzalez-chamorro@newcastle.ac.uk

# Additional identifiers

**Integrated Research Application System (IRAS)**
305745

**Central Portfolio Management System (CPMS)**
51417

**Protocol serial number**
NU-003493

# Study information

## Scientific Title
Muscle MRI as a tool to detect glycogen in the skeletal muscles of patients with adult-onset Pompe patients

## Acronym
MRI in Pompe

## Study objectives
Current study objectives as of 11/06/2026:
This study aims to investigate whether carbon-13 magnetic resonance spectroscopy (13C-MR spectroscopy), a specialist MRI technique, can identify and measure glycogen in the skeletal muscles of people with Pompe disease. The study will also assess whether muscle MRI findings relate to muscle function and whether this technique could be used as a non-invasive biomarker to monitor disease progression and response to treatment.

Previous study objectives:
It is hypothesized that 13C spectroscopy can quantify skeletal muscle glycogen content in patients with Pompe disease.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
1. Approved 24/01/2022, Yorkshire & The Humber - Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 972 2504, +44 (0)207 104 8134; leedswest.rec@hra.nhs.uk), ref: 21/YH/0297
2. Approved 23/09/2025, Yorkshire & The Humber - Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 972 2504; +44 (0)207 104 8134; leedswest.rec@hra.nhs.uk), ref: 21/YH/0297

## Primary study design
Observational

## Study design
Single-centre prospective observational cohort study

## Study type(s)
Diagnostic

## Health condition(s) or problem(s) studied
Pompe disease in adult-onset patients

## Interventions
Current interventions as of 11/06/2026:
This is an observational study. Participants do not receive a study treatment as part of the study and are not randomised into different groups.

The study has two recruitment phases:
1. Original recruitment phase, now completed
This phase included 10 people with Pompe disease in the early stages of disease progression and 10 healthy volunteers matched by age and sex.
People with Pompe disease attended two study visits: one at the start of the study and one after 12 months. Healthy volunteers attended one baseline visit only.
Study visits included clinical assessment, muscle function tests, patient-reported questionnaires, blood sampling, and MRI scans of the legs. Muscle function tests measured strength and physical performance, such as walking, standing up, squatting, and other movements affected by Pompe disease.

2. Current extension phase
This phase will recruit 5 additional people with late-onset Pompe disease who are at a middle stage of disease progression and are already receiving enzyme replacement therapy (ERT).
All 5 participants will attend a baseline visit and a year 1 visit. These visits will include clinical assessment, muscle function tests, patient-reported questionnaires, blood and urine sampling, and MRI scans of the legs.
Of the 5 participants, 3 will also attend an additional MRI visit 5 to 7 days after one of their usual ERT infusions. This will help the researchers explore whether muscle glycogen changes after treatment.
MRI includes carbon-13 magnetic resonance spectroscopy (13C-MR spectroscopy), a specialist MRI technique used to detect glycogen in muscle. The MRI scans also measure muscle water and fat. Some participants will also have additional MRI measurements using a new larger 12 cm carbon coil, which will be compared with the previous 6 cm coil to assess whether it improves glycogen measurement in deeper muscles.

Previous interventions:
This study will consist of clinical assessments, collection of blood samples, a series of muscle function tests and collection of patient-reported outcome measures. The participants with Pompe disease will attend two visits over 1 year (baseline and year 1).

13C-magnetic resonance spectroscopy offers a non-invasive measurement by direct MRI-based detection of a unique signal from natural abundance 13C in glycogen. T2 sequence of muscle water will be obtained from the same MRI as well.

## Intervention Type
Other

## Primary outcome(s)
Current primary outcomes as of 11/06/2026:
Skeletal muscle glycogen content measured using carbon-13 magnetic resonance spectroscopy (13C-MR spectroscopy) during MRI scans of the thighs, at baseline in people with Pompe disease and healthy volunteers, and at the 12-month visit in people with Pompe disease only

Previous primary outcomes:
Glycogen measured using 13C spectroscopy for patients and controls at baseline and at the 12-month visit for patients only

## Key secondary outcome(s)
Current secondary outcomes as of 11/06/2026:
1. Differences in glycogen distribution between anterior and posterior thigh muscles, assessed

using 13C-MR spectroscopy at all the same timepoints used to measure skeletal muscle glycogen content, in people with Pompe disease and healthy volunteers
2. Short-term change in skeletal muscle glycogen content, measured using 13C-MR spectroscopy, before and 5 -7 days after usual enzyme replacement therapy (ERT) infusion in the subgroup of 3 ERT-treated participants
3. Performance and reproducibility of the new 12 cm carbon-13 coil compared with the existing 6 cm carbon-13 coil for measuring skeletal muscle glycogen content, assessed by comparing paired 13C-MR spectroscopy measurements acquired with both coils during the same baseline /pre-infusion MRI visit in the subgroup of 3 ERT-treated participants
4. Muscle water T2 measured using MRI at baseline in people with Pompe disease and healthy volunteers, and at the 12-month visit in people with Pompe disease only
5. Muscle function measured using muscle strength and muscle performance tests at baseline in people with Pompe disease and healthy volunteers and at the 12-month visit in people with Pompe disease only

Previous secondary outcomes:
1. Water accumulation measured using water T2 sequence at baseline for patients and controls and at the 12-month visit for patients only
2. Muscle function measured using muscle strength and performance tests at baseline for patients and controls and at 12 months for patients only

### Completion date
31/12/2028

## Eligibility

### Key inclusion criteria
Updated 11/06/2026:
This study has two recruitment phases. The original recruitment phase included people with Pompe disease in the early stages of disease progression and healthy volunteers matched by age and sex. This phase is now completed. The current extension phase is recruiting 5 additional people with late-onset Pompe disease.

Current inclusion criteria as of 14/07/2025:
Current extension phase:
Five (5) patients with late-onset Pompe disease:
1. People with a diagnosis of Pompe disease, confirmed by reduced enzyme activity and/or genetic testing showing mutations in the GAA gene
2. Aged 12 years or older
3. No contraindications to MRI, meaning there is no medical or safety reason why the person cannot have an MRI scan
4. Willing to complete muscle function tests at the baseline study visit and at the year 1 visit
5. The current extension phase is focused on people with late-onset Pompe disease at a middle stage of disease progression who are already receiving enzyme replacement therapy (ERT)

Healthy volunteers:
Healthy volunteers are not being recruited during the current extension phase. Healthy volunteer recruitment was completed during the original recruitment phase.

Original recruitment phase now completed, for information only:

Ten (10) patients with late-onset Pompe disease:
1. People with a diagnosis of Pompe disease, confirmed by reduced enzyme activity and/or genetic testing showing mutations in the GAA gene
2. Aged 12 years or older
3. No contraindications to MRI
4. No symptoms of muscle weakness or mild symptoms only
5. Willing to complete muscle function tests at the first study visit and at the year 1 visit

Ten (10) healthy volunteers:
1. Male and female healthy volunteers matched by age and sex with the patients with Pompe disease, aged 12 years or older.
2. No contraindications to MRI
3. Willing to complete all study assessments

Previous inclusion criteria as of 05/04/2024:
Patients:
1. Diagnosis of 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 following the diagnostic
2. Aged 12 years and older
3. No contraindications to MRI
4. No symptoms of muscle weakness or mild symptoms
5. Willingness to complete all muscle function tests at baseline and year 1 visit

Healthy controls:
1. Male and female age-matched with the patients (12 years and older)
2. No contraindications to MRI
3. Willingness to complete all study assessments

Previous inclusion criteria:
Patients:
1. Diagnosis of 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 following the diagnostic
2. Aged 12 years and older
3. No contraindications to MRI
4. No symptoms of muscle weakness or mild symptoms. Patients should score higher than 30 points on the RPact scale
5. Willingness to complete all muscle function tests at baseline and year 1 visit

Healthy controls:
1. Male and female age-matched with the patients (12 years and older)
2. No contraindications to MRI
3. Willingness to complete all study assessments

## Participant type(s)
Mixed

## Healthy volunteers allowed
Yes

## Age group

Mixed

### Lower age limit
12 Years

### Upper age limit
120 Years

### Sex
All

### Total final enrolment
0

### Key exclusion criteria
Current exclusion criteria as of 11/06/2026:
1. Contraindications for MRI such as having a metallic prosthesis, pacemaker or any other device that makes the completion of an MRI impossible
2. Not willing to complete all muscle function tests both at baseline and year 1
3. Having claustrophobia or other condition that could limit the capacity of the patient for being located inside the MRI
4. Inability to lie supine during less than 1 hour
5. Pregnancy (for female participants of childbearing age only)
6. Study team decision that it is not in the best interests of the patient to participate in the study

Previous 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. Not willing to complete all muscle function tests both at baseline and year 1 (just patients)
3. Having claustrophobia or other condition that could limit the capacity of the patient for being located inside the MRI
4. Inability to lie supine for less than 45 min
5. Pregnancy (for female participants of childbearing age only)
6. Not being able to understand and speak English (added 17/01/2023: unless accompanied by a translator)
7. Study team decision that it is not in the best interests of the patient to participate in the study

### Date of first enrolment
01/06/2022

### Date of final enrolment
31/12/2027

## Locations

### Countries of recruitment
United Kingdom

England

### 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
**The John Walton Muscular Dystrophy Research Centre**
Institute of Genetic Medicine
Newcastle University
Newcastle upon Tyne
England
NE1 3BZ

### Study participating centre
**Newcastle Magnetic Resonance Centre**
Campus for Ageing and Vitality
Newcastle University
Newcastle upon Tyne
England
NE4 5PL

### Study participating centre
**NIHR Newcastle Clinical Research Facility**
Level 6 Leazes Wing
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
England
NE1 4LP

## Sponsor information

### Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

### ROR
https://ror.org/05p40t847

# Funder(s)

**Funder type**
Industry

**Funder Name**
Sanofi

**Alternative Name(s)**
sanofi-aventis, Sanofi US, Sanofi-Aventis U.S. LLC, Sanofi U.S.

**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

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 26/07/2023 | No | No |
| Participant information sheet | version 1.1 | 14/01/2022 | 23/06/2022 | No | Yes |
| Participant information sheet | version 1.1 | 14/01/2022 | 23/06/2022 | No | Yes |
| Participant information sheet | version 1.1 | 14/01/2022 | 23/06/2022 | No | Yes |
| Participant information sheet | version 1.1 | 14/01/2022 | 23/06/2022 | No | Yes |
| Participant information sheet | version 1.1 | 14/01/2022 | 23/06/2022 | No | Yes |
| Participant information sheet | version 1.1 | 14/01/2022 | 23/06/2022 | No | Yes |
| Participant information sheet | version 2.0 | 04/04/2023 | 05/04/2024 | No | Yes |
| Participant information sheet | version 2.0 | 04/04/2023 | 05/04/2024 | No | Yes |

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|---|---|---|---|---|---|
| Participant information sheet | version 2.0 | 04/04/2023 | 05/04/2024 | No | Yes |
| Participant information sheet | version 2.0 | 04/04/2023 | 05/04/2024 | No | Yes |
| Participant information sheet | version 2.0 | 04/04/2023 | 05/04/2024 | No | Yes |
| Participant information sheet | version 2.0 | 04/04/2023 | 05/04/2024 | No | Yes |
| Participant information sheet | version 3.0 | 28/07/2025 | 11/06/2026 | No | Yes |
| Participant information sheet | version 3.0 | 28/07/2025 | 11/06/2026 | No | Yes |
| Participant information sheet | version 3.0 | 18/07/2025 | 11/06/2026 | No | Yes |
| Protocol file | version 1.0 | 20/10/2021 | 23/06/2022 | No | No |
| Protocol file | version 2.0 | 04/04/2023 | 05/04/2024 | No | No |
| Protocol file | version 3 | 14/07/2025 | 11/06/2026 | No | No |