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# A study to determine the best measurements for patients with ryanodine receptor 1-related muscle disorders

**Submission date**
29/04/2024

**Recruitment status**
No longer recruiting

**Registration date**
15/05/2024

**Overall study status**
Completed

**Last Edited**
16/05/2025

**Condition category**
Genetic Diseases

[_] 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
Ryanodine receptor 1-related myopathies (RYR1-RM) are rare diseases that result in a wide range of symptoms including muscle weakness, pain and fatigue. Individuals are born with RYR1-RM, inheriting either a gene mutation from one or both parents (which affects the severity of the disease) or through spontaneous mutation within the DNA of the gene. There is no current treatment available. ARM210 is a new medication that is being tested as a treatment for these patients. The treatment is safe in healthy volunteers thus far, is progressing through clinical trials and is soon to be tested in patients with RYR1-RM. This study aims to test the strength of muscles in patients with RYR1-RM so that researchers can understand how much these muscles are affected by the disease, and how to measure a consistent result of muscle strength (baseline strength) to inform the design of future clinical trials.

Who can participate?
Adult RYR1-RM patients aged 18 years old and older at screening

What does the study involve?
This study will involve up to 4 visits to a specialist treatment centre over 3 months to undergo study assessments. This will include muscle strength measurements conducted by trained medical staff, the use of a wearable device to track activity and movements for 1 month during the study and answering questions about symptoms caused by the disease including tiredness and pain. There will be no treatment provided as part of this study.

What are the possible benefits and risks of participating?
The results from this study will be used to inform further studies, including the clinical trial to test new treatments for patients with RYR1-RM. The possible risks include that the muscle strength tests - QMA, HHD and MMT may cause discomfort or muscle fatigue in patients but are generally considered low-risk.

Where is the study run from?
RyCarma Therapeutics Inc. (United States)

When is the study starting and how long is it expected to run for?
June 2023 to May 2025

Who is funding the study?
RyCarma Therapeutics Inc. (United States)

Who is the main contact?
Prof. Rosaline Quinlivan, r.quinlivan@ucl.ac.uk

# Contact information

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Public

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# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number
332878

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
CL-EPI-001, IRAS 332878

# Study information

### Scientific Title
An observational study in participants with ryanodine receptor 1-related myopathies (RYR1-RM) to determine optimal endpoint measurements

### Acronym
RYR1 EP

### Study objectives
This study aims to assess the extent to which the strength of proximal muscle movements is affected in patients with RYR1-RM with autosomal dominant mutations and the number of measurements for these movements to establish a stable baseline of the strength in these patients.

### Ethics approval required
Ethics approval required

### Ethics approval(s)
1. Approved 19/02/2024, Health Research Authority and North West - Preston Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; +44 (0)2071048364; approvals@hra.nhs.uk), ref: 24/NW/0022

2. Approved 30/07/2024, METC East Netherlands and CMO Radboud university medical center (METC Oost-Nederland en CMO Radboudumc Gebouw Tandheelkunde, Nijmegen, 6500, Netherlands; +31 (024) 361 31 54; METCoost-en-CMO@radboudumc.nl), ref: 2024-17184

3. Approved 04/07/2024, Comité de protection des personnes Ile de France I (Hôpital Hôtel Dieu - 1, place du Parvis Notre dame 75004 PARIS France, Paris, 75004, France; +33 0142348052; RIPH@sante.fr), ref: 24.01418.000306

### Study design
Observational strength measurement study

## Primary study design
Observational

## Secondary study design
Cohort study

## Study setting(s)
Hospital, Medical and other records

## Study type(s)
Screening

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

## Health condition(s) or problem(s) studied
Ryanodine receptor 1-related myopathies with autosomal dominant mutations

## Interventions
This is an observational, prospective, multi-centre study to assess muscle strength in patients with RYR1-RM with autosomal dominant mutations. The study aims to determine the optimal endpoints for these muscle strength measurements for future studies.

The study will consist of up to four visits:
1. Screening Visit conducted at baseline
2. Visit 1 (30 ± 3 days)
3. Visit 2 (60 ± 3 days)
4. End of Study (EOS) Visit (90 ± 3 days).

Six muscle movements will be tested at each visit to inform optimal endpoints. These will include shoulder abduction, elbow flexion and extension, knee flexion and extension and neck flexion. All except neck flexion will be measured using Quantitative Muscle Assessment (QMA). Neck flexion will be measured using Hand-Held Dynamometry (HHD) and Manual Muscle Testing (MMT). Patients will also be asked to wear a medical device to passively monitor their activity in terms of mobility. This device will be fitted during the screening visit and worn for 1 month only. In addition to QMA, HHD and MMT, additional assessments to be carried out and corresponding timepoints are outlined below:
1. Quantitative muscle assessment, hand-held dynamometry and manual muscle test (Screening, V1, V2, EOS)
2. 10-meter walk test (Screening, V1, V2, EOS)
3. 1 Minute Sit-to-stand test (Screening, V1, V2, EOS)
4. 4 Stair-climb test (Screening, V1, V2, EOS)
5. Questionnaires (International Physical Activity Questionnaire [IPAQ], PROMIS measures of physical function and fatigue) (Screening, EOS)
6. Symptom diary (Screening, EOS)
7. Neurological/physical assessment (Screening, EOS)
8. Wearable device (Fitted at Screening, removed at V1)

The assessments will be carried out by physiotherapists, neurologists or biomedical scientists (depending on which site) at the sites. They will already have training or will receive appropriate training (i.e. for QMA) before conducting the assessments. The assessments must be done in person on-site where all equipment is accessible and will be done individually during a patient visit. The enrolment period is expected to last 2.5 months and the follow-up period is 3 months. The study's overall duration will be approximately 9-12 months, which will include enrolment, follow-up, data collection, analysis and reporting of results.

### Intervention Type
Mixed

### Primary outcome measure
The following primary outcome variables will be assessed at Screening, V1, V2, and EOS:
1. Knee flexion and extension, elbow flexion and extension, and shoulder abduction measured using a quantitative muscle assessment (QMA)
2. Neck flexion measured using a hand-held dynamometer (HHD) and manual muscle test (MMT)
3. Muscle strength measured using a 10-meter walk test (10-MWT), a 1-minute sit-to-stand test, and a 4-Stair climb test

The study will consist of up to four visits:
1. Screening Visit conducted at baseline
2. Visit 1 (V1: 30 ± 3 days)
3. Visit 2 (V2: 60 ± 3 days)
4. End of Study (EOS) Visit (90 ± 3 days)

### Secondary outcome measures
1. Fatigue and physical function measured using the PROMIS Fatigue, PROMIS-physical function domains at Screening and EOS
2. Physical activity measured using the International Physical Activity Questionnaire (IPAQ) at Screening and EOS
3. Demographics measured using data collected in medical records at screening
4. Clinical characteristics of patients measured using data collected in medical records and full physical assessments at Screening and EOS
5. Syptoms measured using a diary at screening and EOS

The study will consist of up to four visits:
1. Screening Visit conducted at baseline
2. Visit 1 (V1: 30 ± 3 days)
3. Visit 2 (V2: 60 ± 3 days)
4. End of Study (EOS) Visit (90 ± 3 days)

### Overall study start date
14/06/2023

### Completion date
30/05/2025

## Eligibility

### Key inclusion criteria

1. Male and female patients (biological sex*) aged 18 years or older at Screening; Adult males and females aged 18 years and older at Screening
2. Confirmed genetic diagnosis of RYR1-RM with autosomal dominant mutation and supporting clinical phenotype with demonstrable proximal weakness on at least one of the baseline study assessments
3. Evidence of at least one demonstratable muscle/motor function deficit assessed through MMT and scored using the MRC Scale for muscle strength on physical examination
4. Able to walk 10 meters, with or without assistance - e.g., with a cane (assessed using the 10-MWT)
5. Willingness and ability to comply with scheduled visits, and study procedures
6. Willingness to be fitted with the Syde® device at Screening Visit (for inclusion in the exploratory objective only)
7. Able to provide written informed consent and understand the study procedures in the informed consent form (ICF)

## Participant type(s)
Patient

## Age group
Mixed

## Lower age limit
18 Years

## Upper age limit
100 Years

## Sex
Both

## Target number of participants
20

## Total final enrolment
8

## Key exclusion criteria
Participants meeting at least one of the following criteria will not be eligible for the study:
1. Severe pulmonary dysfunction at Screening (FVC < 40% predicted) or evidence of pulmonary exacerbation (note that pulmonary exacerbations refer to acute worsening respiratory symptoms resulting from a decline in lung function)
2. Significant cognitive impairment in the judgement of the investigator who will be unable to follow the protocol
3. Patients with progressive neurological conditions (e.g., Parkinson’s disease)
4. Non-ambulant patients
5. Pregnant women

## Date of first enrolment
13/05/2024

## Date of final enrolment

28/02/2025

# Locations

### Countries of recruitment
England

France

Netherlands

United Kingdom

### Study participating centre
**University College London Hospitals NHS Foundation Trust**
250 Euston Road
London
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NW1 2PG

### Study participating centre
**Radboud University Medical Centre**
Clinical Research Unit, Route 923, Geert Grooteplein Zuid 10
Nijmegen
Netherlands
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### Study participating centre
**Association Institut de Myologie**
Association Institut de Myologie, Groupe Hospitalier Pitié-Salpêtrière, Bâtiment Babinski RDC bas,
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# Sponsor information

### Organisation
RyCarma Therapeutics Inc.

### Sponsor details

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### Sponsor type
Industry

## Funder(s)

### Funder type
Industry

### Funder Name
RyCarma Therapeutics Inc.

## Results and Publications

### Publication and dissemination plan
Planned publication in a peer-reviewed journal

### Intention to publish date
01/09/2026

### Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

### 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? |
|---|---|---|---|---|---|
| Protocol file | version 4.0 | 10/09/2024 | 17/10/2024 | No | No |