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

Submission date	Recruitment status No longer recruiting	Prospectively registered		
29/04/2024		[X] Protocol		
Registration date	Overall study status Completed Condition category	Statistical analysis plan		
15/05/2024		Results		
Last Edited		Individual participant data		
16/05/2025	Genetic Diseases	[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

Type(s)

Public

Contact name

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Type(s)

Principal Investigator

Contact name

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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 \pm 3 days)
- 3. Visit 2 ($60 \pm 3 \text{ days}$)
- 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: $30 \pm 3 \text{ days}$)
- 3. Visit 2 (V2: $60 \pm 3 \text{ days}$)
- 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: $30 \pm 3 \text{ days}$)
- 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

Locations

Countries of recruitment

England

France

Netherlands

United Kingdom

Study participating centre University College London Hospitals NHS Foundation Trust

250 Euston Road London United Kingdom NW1 2PG

Study participating centre Radboud University Medical Centre

Clinical Research Unit, Route 923, Geert Grooteplein Zuid 10 Nijmegen Netherlands 6525

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

200 Clarendon Street, 22nd Floor Boston United States of America MA 02116 +1-888-209-5458 contact@rycarma.com

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