ISRCTN29338211 https://doi.org/10.1186/ISRCTN29338211

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

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
332878

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Screening

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(s)

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)

Key secondary outcome(s))
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)

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

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

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
United Kingdom

England

France

Netherlands

Study participating centre

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Sponsor information

Organisation
RyCarma Therapeutics Inc.

Funder(s)

Funder type
Industry

Funder Name
RyCarma Therapeutics Inc.

Results and Publications

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