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An observational longitudinal study of congenital myasthenic syndromes

Submission date
06/10/2022

Recruitment status
No longer recruiting

Registration date
28/11/2022

Overall study status
Completed

Last Edited
21/10/2025

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Congenital myasthenic syndromes are characterized by muscle weakness (myasthenia) that worsens with physical exertion. The Oxford Highly Specialist CMS Service is running an observational natural history study to help understand the symptoms and problems people with congenital myasthenic syndromes (CMS) have. The researchers will do this by measuring muscle strength and fatigue and completing different questionnaires with participants. They can then compare which assessment scales are most suitable for people with different genetic subtypes. This will support future patient clinical care and help us to design future clinical treatment trials.

Who can participate?
Patients aged 0-100 years with a confirmed genetic diagnosis of CMS who attend the Oxford CMS centre for their study and clinical appointments for the duration of this study

What does the study involve?
All assessments will be completed alongside the participant's CMS clinic appointment in Oxford and will involve assessments that are part of a normal clinic review. As part of this study, participants will be asked to complete additional assessments, including physical exercises and questionnaires, plus optional assessments such as patient self-assessments to be completed at home and wearing an activity monitor. To complete these additional assessments the visit may take longer than usual, which could be up to 2 hours on average. The frequency of clinic appointments may increase, to ensure that participants are seen every 6 months, throughout the duration of the study.

What are the possible benefits and risks of participating?
There is no direct benefit to taking part, but this study will aid with the wider understanding of CMS. This is an observational study, and as such does not include any intervention. However, the study design involves completing a number of physical assessments to assess muscle fatigue and as a result may cause temporary muscle weakness. The researcher completing the assessments will mitigate this as far as possible by allowing rest breaks between assessments where able.

When is the study starting and how long is it expected to run for?
April 2020 to May 2024

Who is funding the study?
Amplo Biotechnology Inc. (USA)

Who is the main contact?
Hayley Ramjattan, orh-tr.cmsgenetics@nhs.net

Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
289835

Protocol serial number
1/090421

Study information

Scientific Title
A natural history study of congenital myasthenic syndromes to establish reliable outcome measures suitable for clinical and research assessment

Study objectives
To identify relevant and reliable outcome measures for assessing and monitoring change in the congenital myasthenic syndromes (CMS) population within the UK.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 05/01/2022, London - Bromley Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, UK; +44 (0)207 104 8063; bromley.rec@hra.nhs.uk), ref: 21/LO/0480

Primary study design
Observational

Study design
Observational exploratory study

Study type(s)
Other

Health condition(s) or problem(s) studied
Congenital myasthenic syndromes (CMS)

Interventions
This is an observational exploratory study, conducted within the Oxford CMS clinic appointment, forming part of routine patient care. This study is expected to last for 24 months, with recruitment in the first 6 months. Each participant will be followed up at 6 monthly intervals, which aligns with the majority of the patient's clinical visits. This will aim to include 2-4 visits (including baseline).

All assessments will be completed alongside the participant's CMS clinic appointment in Oxford and will involve assessments that are part of a normal clinic review. As part of this study, participants will be asked to complete additional assessments, including physical exercises and questionnaires, plus optional assessments such as patient self-assessments to be completed at home and wearing an activity monitor. To complete these additional assessments the visit may take longer than usual, which could be up to 2 hours on average. The frequency of clinic appointments may increase, to ensure that participants are seen every 6 months, throughout the duration of the study.

Intervention Type
Other

Primary outcome(s)
Muscle fatigue measured using the following assessments: Quantitative Myasthenia Gravis (QMG) score at baseline, 6, 12 and 18 months

Key secondary outcome(s)
Measured at baseline, 6, 12 and 18 months:
1. Muscle fatigue measured using the following assessments: Sit-to-stand in One Minute (STS1M), 10-metre run (10m run), 6-Minute Walk Test (6MWT) and stairs climb (ascend and descend)
2. Activity levels monitored between clinic visits using a wrist-worn accelerometer device (AX3), worn for 7 days post visit and a patient self-assessment diary, completing arm outstretched and STS1M daily at home for 7 days
3. Patient-reported outcome measures:
3.1. Mental wellbeing measured using the Hospital Anxiety and Depression Scale (HADS)
3.2. Physical health measured using EQ-5D-5L
3.3. Participation measured using Myasthenia Gravis Activities of Daily Living (MG-ADL)

4. For children under 4 years of age, motor skill is measured using the CHOP-INTEND and WHO motor milestones
5. The impact on caregivers of supporting an individual with CMS will be measured using the Care Giver Indirect and Informal Care Cost Assessment Questionnaire, completed once in the study by the participant's carer, parent, guardian, or partner (with their direct consent)

Completion date
31/05/2024

Eligibility

Key inclusion criteria
1. Participants with a confirmed genetic diagnosis of CMS, who are referred to the Oxford CMS service for their clinical management
2. 0-100 years of age
3. Participant is willing and able to give informed consent for participation in the study
4. The participant must be able to understand written and spoken English
5. Able to attend clinic every 6 months for face-to-face assessment with a physiotherapist

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Lower age limit
0 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
50

Key exclusion criteria
1. Non-CMS medically or psychological conditions that may affect the OCMs, as judged by the medical team
2. Participants not compliant/unable to attend regular reviews in Oxford
3. Participants involved in other CMS research (e.g. novel therapies), which may impact the study assessments

Date of first enrolment
04/02/2022

Date of final enrolment
08/03/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
Oxford University Hospitals NHS Trust

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Industry

Funder Name
Amplo Biotechnology Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository. Data will be stored on the CMS Tissue Bank clinical database (CMS TB database), which is the clinical database established for the CMS service. This database is held

on REDCAP. Only designated members of the CMS clinical team and study team will have access. All the participants in the study will need to have already consented to their data being recorded on the CMS TB database as part of routine clinical care. Data will be collected from relevant medical history and physical assessments during their routine clinical visit. Participants will be identified through their CMS TB database reference number. This number will also then be their participant study number, which will be used throughout the study. All data entered into the CMS TB database will be retained for the length of time the participant is a patient under the Oxford CMS service. If they leave the service, participants will be offered the option for their data to remain part of the CMS TB database for longer-term analysis.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		21/10/2025	21/10/2025	No	No
HRA research summary			28/06/2023	No	No