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Long-term follow-up of heart function in participants of the Duchenne Muscular Dystrophy Heart Protection study

Submission date
17/04/2023

Recruitment status
No longer recruiting

Registration date
11/09/2023

Overall study status
Completed

Last Edited
26/08/2025

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Almost all boys with Duchenne muscular dystrophy (DMD) develop progressive cardiomyopathy. The DMD Heart-Protection Study (https://www.isrctn.com/ISRCTN50395346) tested whether starting perindopril and bisoprolol in combination before evidence of dysfunction of the heart muscle (ventricular dysfunction) could delay the onset of cardiomyopathy. The study ended in 2018 after 75 boys had been studied for 3 years. Although left ventricular dysfunction did occur in some participants, there was not a group benefit for active therapy in the primary endpoint. This may be explained by the fact that most participants were also getting the benefits of maintenance steroids combined with inter-patient variability in the age of cardiomyopathy onset meaning that longer follow-up data are needed to show outcome differences. This study aims to reanalyse data between the groups from baseline after adding 2-3 years of further data obtained from normal NHS review to the original dataset. No additional testing or hospital visits are required. International experts and patient group advocates agree on the importance of longer follow-up of this patient cohort to determine the role of prophylactic heart therapy in young boys with DMD.

Who can participate?
Males with DMD who participated in the original DMD Heart Protection study

What does the study involve?
This 'follow-on' study aims to collect and analyse heart measurements from evaluations done on the original participants for longer (eg: extend the minimum follow-up to 5 years) and re-analyse according to what treatment participants were randomized to originally. Males with DMD typically have heart assessments annually. This study does not require any additional testing or hospital visits for patients/families but does require re-consenting to allow the data accumulated since each participant exited the study to be transferred securely from clinical teams caring for these patients to researchers. Participants were all recommended active heart treatments as they exited the DMD Heart Protection Study. So, those originally taking 'dummy' drugs during the study have also been on unblinded active therapy since then.

Because best practice recommendations, developed by consensus since this study ended, now recommend prophylactic heart therapy empirically from age 10 years, it will not be possible to conduct a further placebo-controlled study of this kind. Therefore, extending follow-up in the DMD Heart-Protection cohort provides a unique opportunity to determine whether it is better to start a combination of heart drugs at a younger age in boys with DMD, while heart function is still healthy than starting the same drugs 3-5 years later with the onset of ventricular dysfunction. Collating and reanalysing these additional measures are central to establishing the evidence-base underpinning recently updated international recommendations on the use of conventional heart drugs prophylactically in boys with DMD.

What are the possible benefits and risks of participating?
No benefits will accrue to individual participants. The findings should clarify the indeterminate results at the end of the three-year follow-up from the original study. Crucially, the longer-term findings are expected to establish the clinical utility of introducing two heart medications prophylactically in combination in young males with DMD to slow the development of cardiomyopathy. No risks are anticipated for participants or carers, and none have been identified.

Where is the study run from?
Newcastle upon Tyne NHS Hospitals Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
December 2020 to July 2023

Who is funding the study?
Duchenne UK (UK)

Who is the main contact?
Dr JP Bourke, john.bourke@nhs.net (UK)

Contact information

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Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
269110

Central Portfolio Management System (CPMS)
49264

Protocol serial number
09825

Study information

Scientific Title
Long-term follow-up of heart function in participants of the Duchenne Muscular Dystrophy Heart Protection study

Acronym
DMD Heart Protection study follow-up

Study objectives
The null hypothesis is that prophylactic therapy with an ACE-inhibitor (perindopril) and beta-blocker (bisoprolol) in combination will neither delay the onset nor slow the rate of progression of left ventricular systolic dysfunction compared to placebo over five to six years of follow-up.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/06/2021, London - Brent Research Ethics Committee (80 London Road, Skipton House, London, SE1 6LH, UK; +44 (0)20 7104 8128, (0)20 7104 8137; brent.rec@hra.nhs.uk), ref: 21/PR/0595

Primary study design
Observational

Study design
Observational study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Duchenne muscular dystrophy-related cardiomyopathy

Interventions
Almost all boys with Duchenne muscular dystrophy (DMD) develop progressive cardiomyopathy. The prior multicentre, randomized, placebo-controlled, Heart-Protection Study ['A double-blind randomized, multi-center, placebo-controlled trial of combined ACE-inhibitor and beta-blocker therapy in preventing cardiomyopathy in genetically characterized males with DMD without echo-detectable left ventricular dysfunction'] (LV) tested whether starting perindopril and bisoprolol in combination before evidence of LV dysfunction could delay the onset of cardiomyopathy. The study ended in 2018 after 75 boys had been studied for three years. Although LV dysfunction did occur in some participants, there was not a group benefit for active therapy in the primary endpoint (ie: change in LVEF% from baseline). This may be explained by the fact that most participants were also getting the benefits of maintenance steroids and this, combined with inter-patient variability in the age of cardiomyopathy onset, meaning that longer follow-up was needed to show outcome differences. This proposal aims to reanalyse the change in LVEF% between groups from baseline after adding 2-3 years of data, obtained from normal NHS review, to the original dataset. No additional testing or hospital visits are required. International experts and patient group advocates agree on the importance of longer follow-up of this patient cohort to determine the role of prophylactic heart therapy in young boys with DMD.

Measures of exposure
International Standards of Care recommend that patients with DMD undergo cardiac testing at least annually as part of routine NHS care. This extension / 'follow-on' phase simply aims to collect and analyse heart test results from heart scans done on the original participants since their participation in the DMD Heart Protection study ended, add the extra serial measures to the original data set and re-compare the groups according to their initial treatment randomization ('active' vs 'placebo'). The proposal does not require any additional testing or hospital visits for patients/families.

Primary outcome measure / Follow-up duration
Change in LV ejection fraction from original study enrolment ('baseline') after a minimum follow-up of five years from initial recruitment (2011-2015). The study team expects to have a 6-year follow-up with most participants.

Proposed sample size/power calculation / lost to follow-up
The sample size is dictated by the original number of participants [n=85], the number who continued to study end [n=75] and those who will provide consent. Some will have transitioned from paediatric to adult cardiology care and results will be obtained from wherever heart tests were undertaken.

Intervention Type
Other

Primary outcome(s)
Change in echocardiogram-measured left ventricular ejection fraction measured using electronic medical records from initial recruitment to study end

Key secondary outcome(s)

1. Change in left ventricular fractional shortening and left ventricular chamber dimensions measured using electronic medical records from initial recruitment to study end
2. Sub-group analysis may be measured using electronic medical records from initial recruitment to study end. Pre-specified sub-group analyses may include:
2.1. Steroid use versus steroid naive patients
2.2. Actual therapy received since original study exit
2.3. Participant age at onset of detectable cardiomyopathy
2.4 Use of other DMD-modifying therapies (ie: exon skipping; ataluren; adenovirus gene therapy or similar).

Completion date
30/07/2023

Eligibility

Key inclusion criteria
1. Participated in the original DMD Heart Protection study (https://www.isrctn.com/ISRCTN50395346)
2. Valid consent of boys/parent or carer (age dependent) to allow access to serial measures of heart function and limited other data wherever undertaken, from the time each participant exited the original study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Sex
Male

Key exclusion criteria
1. Did not participate in the original DMD Heart Protection study
2. Refusal of re-consent

Date of first enrolment
10/01/2022

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Newcastle upon Tyne Hospitals NHS Foundation Trust - Comcov2 Covid19 Trials
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Dubowitz Neuromuscular Centre
UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital for Children NHS Foundation Trust
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Study participating centre
Alder Hey Children's NHS Foundation Trust
Radiant House
28-30 Fowler Road
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Study participating centre
Heart of England NHS Foundation Trust, Birmingham
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Sponsor information

Organisation
Duchenne UK

Funder(s)

Funder type
Charity

Funder Name
Duchenne Research Fund

Alternative Name(s)
Duchenne UK, THE DUCHENNE RESEARCH FUND, DRF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study are not expected to be made available. However, they may be provided on special request to the chief investigator (john.bourke@nhs.net) or to the study statistician (andy.bryant@newcastle.ac.uk) on a case-by-case decision basis until 20th December 2026.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/03/2025	19/08/2025	Yes	No