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Repurposing empagliflozin for Duchenne muscular dystrophy-associated cardiomyopathy in children 6-18 years of age

Submission date 23/04/2025	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 27/08/2025	**Overall study status** Ongoing	
Last Edited 27/08/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

Cardiac disease is a major cause of death in Duchenne muscular dystrophy. It is important to recognise and address this early in the disease course, i.e. during childhood/adolescence. Sadly, current heart failure therapy in paediatrics is still unsatisfactory. Fortunately, however, some advances are in the pipeline. Indeed, this study aims to repurpose empagliflozin for DMD-associated cardiomyopathy, a novel molecule that demonstrated impressive benefits in adults with heart failure. Trials in pediatric heart failure have hitherto often failed because of suboptimal dose, inappropriate formulations or inadequate endpoints. This study will take advantage of the power of pharmacokinetic modelling and simulation to address these issues with a stepwise, translational approach. In adults, empagliflozin has recently been found to reduce death or worsening heart failure by 25%, on top of optimal medical therapy. So far, paediatric studies on SGLT2 inhibitors have focused on diabetes mellitus (adolescents) and glycogen storage disease type Ib (children). Safety studies in children have been reassuring. However, little is known about their use in children or adolescents with DMD-associated cardiomyopathy. Leveraging prior knowledge from available studies and developmental pharmacology, this study will define the dose rationale, assess safety and ease of swallowing, and explore the efficacy of empagliflozin among children/adolescents with DMD-associated cardiomyopathy.

Who can participate?

Children/adolescents with DMD-associated cardiomyopathy 6-18 years of age, currently on heart failure drug therapy

What does the study involve?

Participants will receive empagliflozin for 6 months and will have 5 study visits (Visit 1 and follow-up visits at 1 week, 6 weeks, 3 and 6 months), and one end-of-study visit 2-12 weeks after having completed the trial. Visit 1 will imply a one-day stay (8 hours) in the clinical research facility of the paediatric hospital, whilst Visits 2-5 will be similar to regular heart failure clinics. Safety evaluation will occur throughout the study, ease-of-swallow will be evaluated at Visit 1, and efficacy markers (clinical examination, bloods, echocardiography, cardiac magnetic

resonance) at Visits 1 and 5. Advanced calculations (pharmacokinetic modelling) will allow the definition of the optimal dose in DMD children and adolescents, informing both current compassionate-care clinical use and the design of subsequent efficacy trials.

What are the possible benefits and risks of participating?
The main potential side effects related to receiving empagliflozin are the development of low blood sugar, high blood ketones, metabolic acidosis, renal function deterioration, dehydration or genito-urinary infections. To limit these risks, patients with diabetes mellitus or other diseases predisposing to low blood sugar will not be included in this study. Furthermore, renal function, blood glucose, blood gas and ketones, and urinary dipsticks will be repeatedly checked, to make sure any derangement will be timely assessed and managed.

Where is the study run from?
Great Ormond Street Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2025 to March 2027

Who is funding the study?
Duchenne UK

Who is the main contact?
GOSH R&D CTIMPs Team, rdctimpsteam@gosh.nhs.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2024-000201-33

IRAS number
1009946

ClinicalTrials.gov number
NCT06643442

Secondary identifying numbers
24HL14

Study information

Scientific Title
Repurposing empagliflozin for Duchenne muscular dystrophy-associated cardiomyopathy in children: a pharmacokinetics, safety and proof-of-concept study among children 6-18 years of age

Acronym
REDMeD

Study objectives

Primary objectives:
To characterize the pharmacokinetics of empagliflozin (one of the two SGLT2 inhibitors currently recommended for adults with heart failure, with or without diabetes mellitus) in children and adolescents with Duchenne muscular dystrophy (DMD)-associated cardiomyopathy.

Secondary objectives:
1. Assess ease of swallow
2. Monitor safety
3. Explore several potential markers of efficacy, which might be used in future efficacy trials

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/06/2025, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8241; hampstead.rec@hra.nhs.uk), ref: 25/LO/0361

Study design
Pharmacokinetics safety proof-of-concept study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Safety

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

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

Interventions
Empagliflozin 10 mg once daily (commercially available tablets: Jardiance 10 mg film-coated tablets) p.o. once daily for 6 months

Follow-up visits: visit 1, visit 2 (week 1), visit 3 (week 6), visit 4 (month 3), visit 5 (month 6), end-study visit (2-12 weeks after study end/visit 5).

Intervention Type
Drug

Pharmaceutical study type(s)

Pharmacokinetic, Therapy

Phase
Phase II

Drug/device/biological/vaccine name(s)
Empagliflozin

Primary outcome measure
The concentration of empagliflozin at different time-points after drug intake: 6 PK samples at Visit 1 (day 1), 1 sample at Visit 2 (week 1) and 1 sample in at least half of the participants at Visit 3 (week 6). The specific time points will be different, with 4 sampling groups of 3 patients each. The specific sampling times are available on request.

Based on these concentrations, pharmacokinetic calculations will be performed, allowing the determination of pharmacokinetic parameters:
1.1. Apparent clearance (CL/F)
1.2. Central volume of distribution (Vd/F)
1.3. Half-life (t1/2)
1.4. Area-under-the-concentration-time curve (AUC)
1.5. Maximal concentration (Cmax)

Secondary outcome measures
1. Ease of swallow (facial hedonic scales with 4 possible answers): at Visit 1, shortly after first drug intake.

Safety:
2.1. eGFR
2.2. Occurrence of hypoglycemia
2.3. Occurrence of ketoacidosis
2.4. Occurrence of UTI
2.5. History of adverse events
Timing: Visit 1 to Visit 5 (Visit 1 = day 1, Visit 2 = 1 week, Visit 3 = 5–6 weeks, Visit 4 = 3 months, Visit 5 = 6 months after enrolment).

Efficacy and efficacy markers:
3.1. Heart failure severity class (NYHA if ≥8 years, Ross if <8 years): Visits 1, 4 and 5.
3.2. Patient-reported outcomes
3.2.1. Patient global impression of severity (PGIS): Visits 1, 4 and 5
3.2.2. Patient global impression of change (PGIC): Visits 1, 4 and 5.
3.3. NT-proBNP: Visits 1, 3, 4 and 5.

3.4. Echocardiography:
3.4.1. Left ventricular end-diastolic dimension (LVEDd) absolute dimension and z-score
3.4.2. Left ventricular end-systolic dimension (LVESd) absolute dimension and z-score
3.4.3. Fractional shortening (FS)
3.4.4. Left ventricular Ejection fraction (LV-EF)
Timing: Visits 1, 4 and 5.

3.5. Cardiac MRI:
3.5.1. LV end-diastolic volume

3.5.2. LV end-systolic volume
3.5.3. Left ventricular Ejection fraction (LV-EF)
3.5.4. Extracellular volume
3.5.5. Presence (y/n and number of segments) of fibrosis.
Timing: Visits 1 and 5.

3.6. Clinical observations:
3.6.1. Body weight (kg)
3.6.2. Heart rate (/min)
3.6.3. Systolic and diastolic blood pressure (mmHg)
Timing: Visits 1, 4 and 5.

3.7. Circulating biomarkers:
3.7.1. Beta-hydroxybutyrate
3.7.2. Haemoglobin
3.7.3. Uric acid
3.7.4. Na+, K+, Ca2+
3.7.5. Klotho/FGF-23
Timing: Visits 1, 4 and 5.

3.8. Bioimpedance:
3.8.1. Total fluid volume
3.8.2. Intra- and
3.8.3. Extracellular fluid volumes
Timing: Visits 1, 4 and 5.

Visit Schedule:

Visit 1 = Day 1
Visit 2 = 1 week after enrolment
Visit 3 = 5–6 weeks after enrolment
Visit 4 = 3 months after enrolment
Visit 5 = 6 months after enrolment

Overall study start date
17/04/2025

Completion date
31/03/2027

Eligibility

Key inclusion criteria
1. Children or adolescents 6 to 18 years of age with DMD-associated cardiomyopathy, followed either as in- or outpatients at the Heart Failure Unit, Pediatric Cardiology Service, Heart & Lung Directorate, Great Ormond Street Hospital NHS Foundation Trust, London, will be eligible for inclusion.
1.1. Patients with DMD-associated cardiomyopathy, who are currently followed elsewhere, but who, having been made aware of this study (e.g. through other patients they know, parental associations etc) and who would like to participate, may contact the study team with the question of participating. These patients may be considered for eligibility as well. The study

team might want, as an additional inclusion/exclusion criterion, to discuss their participation with their treating paediatric cardiologist.
2. Currently on heart failure medication (any drug or any combination).
3. Patients should potentially benefit from adding an SGLT2i (as judged by the treating physician and the local PI or Co-PI).
4. Patients need to be on stable medical treatment, defined as no new heart failure drug started over the preceding 30 days and no major drug dose modification (apart from minor adaptations, like weight adaptations, rounding or formulation changes) during the 2 weeks prior to enrolment.
5. Adolescents, respectively parents or caregivers of children, capable of giving informed consent (including sufficient development and sufficient understanding, as judged by the local investigator).
6. Ability to tolerate a cardiac MRI investigation without the need for general anaesthesia.

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
12

Key exclusion criteria
1. Inability to understand and go through the informed consent procedure.
2. Inability to receive medications per os or through a nasogastric tube.
3. Type 1 or Type 2 Diabetes mellitus or any underlying metabolic disease associated with hypoglycaemias.
4. Body weight <15 kg (because, basing on pharmacokinetic simulations, available tablets may exceed adult Cmax and/or AUC by >130% (75th percentile of simulated Cmax and/or AUC) in patients below 15 kg weight)
5. Current smokers (defined as >1 cigarette/week).
6. Use of any other nicotine-delivering product (e.g. nicotine patches).
7. Any known illicit drug abuse.
8. Active chronic HBV, HCV or HIV.
9. Any major surgery within 4 weeks of first dose administration.
10. Blood transfusion recipient within 4 weeks of first dose administration.
11. eGFR equal to or less than 45 mL/min/1.73m2 (simplified Schwartz formula, and/or respectively the cystatine C-based Filler equation).
12. K+ >6.5 mmol/L.
13. Blood glucose <4 mmol/L.
14. There are no blood pressure exclusion criteria foreseen, but participants need to be

haemodynamically stable, as assessed by the local investigator.
15. Sustained or symptomatic arrhythmia insufficiently controlled with drug and/or device therapy.
16. Cardio-surgical procedure within the 2 months prior to Visit 1, or interventional cardiac catheterization within 2 weeks prior to Visit 1, or is planned to undergo cardiac surgery or an interventional cardiac catheterization during the study period (i.e. in the 6 months following Visit 1).
17. Post-menarchal female patients (for biological reasons inherent to DMD, this only applies to female carriers or to Becker muscular dystrophy patients) of childbearing potential cannot be included.
18. Females must not be breastfeeding (this criterion is just a legal specification, biologically and clinically it is already implicit in the previous exclusion criterion, since DMD-boys and pre-menarchal girls cannot breastfeed).
19. Known lactose intolerance, galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption (since Jardiance® tablets contain lactose).
20. Known allergies to active ingredients or excipients of Jardiance® tablets.
21. Significant medical history of active (last 6 weeks) severe medical disease (e.g. active oncological disease, sepsis within the preceding 6 weeks, …).
22. Patient on continuous home supplemental oxygen because of chronic pneumopathy.
23. Significant liver disease, Child Pugh Class C, or significant laboratory abnormalities at enrolment (defined as ALT or AST, ALP, γGT or total Bilirubin >3 times the upper limit of normal).
24. Significant gastroenterological or hepatic disease that could significantly impair absorption or metabolism of orally administered drugs.
25. Any medical co-morbidity, which is deemed incompatible (or only with relevant risk) with study participation by the treating clinician and/or the study investigator.
26. Active urinary tract infection (being treated with antibiotics at the moment of Visit 1) or other relevant bacterial infection, as judged by the treating clinician and/or the study investigator.
27. The patient is currently participating in another interventional clinical trial or has participated in such a trial during the <14 days before Visit 1 (or if enrolment in this study is incompatible with the protocol of that preceding trial), or the duration of five half-lives of the IMP, whichever is longer

Date of first enrolment
01/10/2025

Date of final enrolment
30/09/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Great Ormond Street Hospital
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
https://www.ucl.ac.uk/child-health/great-ormond-street-institute-child-health

Funder(s)

Funder type
Charity

Funder Name
Duchenne UK

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

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Conference presentation(s)
3. Publication on website
4. Submission to regulatory authorities
5. Other

Intention to publish date
31/12/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon reasonable written request from interested scientists or clinicians to the sponsor, PI, or co-PI. Only pseudo-anonymized data will be shared, under strict access criteria lasting a maximum of 60 days. This will be subordinated to a specific, a posteriori consent from all participants, and to the respect of all laws and regulations that apply, the study protocol and clauses highlighted in the consent and assent forms.

IPD sharing plan summary
Available on request