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A study to investigate how ENTR-601-44 behaves in the body, the safety and how well tolerated different increasing amounts of the drug ENTR-601-44 are when given to healthy male volunteers

Submission date 16/08/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 16/08/2023	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 06/06/2025	**Condition category** Other	[_] Individual participant data

Plain English summary of protocol

Background and study aims
ENTR-601-44 is being investigated as a drug for Duchenne muscular dystrophy (DMD). The study aims to investigate the safety, how it behaves in the body and how well tolerated different increasing amounts of the drug ENTR-601-44 are when given to healthy male volunteers.

Who can participate?
People who join the study must be healthy men between 18 and 55 years old.

What does the study involve?
The study will test increasing doses of the drug ENTR-601-44 in groups of 8 healthy male volunteers. Four different dose levels will be tested. In each group, 6 participants will receive the drug and 2 will receive a placebo. For each dose group, 2 participants (1 getting the drug and 1 getting a placebo) will be given the dose first. After 7 days, if the drug is safe and tolerated in the first 2 participants, the remaining 6 participants in that group will also receive their doses. Each new dose level will only be tested if the previous level was safe. Participants will be screened for up to 28 days (Visit 1) before the study. They will stay at the clinic (Visit 2 Inpatient stay) from the day before the dose (Day -1) until 7 days after (Day 7). They will have to return for follow-up visits on Day 14 (Visit 3), Day 21 (Visit 4), Day 28 (Visit 5) and Day 42 (Visit 6) after dosing.

What are the possible benefits and risks of participating?
There are no medical benefits to taking part in the study since the trial is in healthy volunteers, but the study will contribute to scientific knowledge which may lead to the expansion of treatment options for people with DMD. The study drug has never been given to people before, so it is unknown what specific side effects might occur. Previous studies in monkeys and mice have shown that there may be effects on the

kidneys when taken at doses much higher than those planned to be administered in this study. These effects were minimal and were shown to be reversible. There will be frequent blood and urine tests to monitor for signs of potential damage to the kidneys. Medications similar to the study drug have been shown to cause a decrease in platelet levels in the blood. Platelets are fragments of cells that help blood to clot and reduce bleeding. Blood tests will be taken throughout the study and platelet levels will be monitored throughout. In addition, the study doctor will examine participants for signs of low platelets during routine physical examinations.

Where is the study run from?
MAC Clinical Research (UK)

When is the study starting and how long is it expected to run for?
July 2023 to August 2024

Who is funding the study?
Entrada Therapeutics, Inc. (USA)

Who is the main contact?
MAC Clinical Research, projectcoordinators@macplc.com

Contact information

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Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1007814

Protocol serial number
MAC Clinical Research: MAC175, ENTR-601-44-101

Study information

Scientific Title
Phase 1 Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate Safety, Tolerability, and Pharmacokinetics of a Single Intravenous Infusion of Ascending Doses of ENTR-601-44 in Healthy Male Volunteers

Study objectives
1. To assess the safety and tolerability of a single dose of ENTR-601-44,
2. To characterize the pharmacokinetic (PK) profile of a single dose of ENTR-601-44 and its major metabolite PMO-0235a,
3. To characterize the pharmacodynamics (PD) of ENTR-601-44

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/07/2023, Wales Research Ethics Committee 1 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)2920 785738; Wales.REC1@wales.nhs.uk), ref: 23/WA/0123

Primary study design
Interventional

Study design

Phase 1 randomized double-blind placebo-controlled trial in a single centre

Study type(s)
Safety

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
This study will consist of a double-blind, randomized, placebo-controlled, single ascending dose design in healthy male volunteers. Approximately 32 participants will be enrolled in the study. Single ascending doses of ENTR-601-44 will be investigated in sequential cohorts comprising 8 healthy male volunteers each. Four dose levels are planned to be investigated. No participant will be a member of more than one treatment group. The planned dose levels to be tested are 0.75 mg/kg (Cohort 1), up to 1.5 mg/kg (Cohort 2), up to 3.0 mg/kg (Cohort 3), up to 6.0 mg/kg (Cohort 4) of ENTR-601-44. Within each cohort, 8 participants will be randomized to receive a single dose of ENTR-601-44 (n = 6) or placebo (n = 2) on Day 1. ENTR-601-44 will be administered as a single IV dose over a 1-hour (± 10 minutes) infusion period. An initial sentinel group of 2 participants will be enrolled for each cohort, of which 1 participant will receive ENTR-601-44 single dose infusion and the other participant will receive placebo. The non-sentinel group will consist of the remaining 6 participants, who will only be dosed after the available 7-day post-dose initial safety data from the sentinel participants are assessed by the Investigator. The total duration of follow up is approximately 6 weeks.
The clinical study will be performed in a double-blind manner. The randomization code will be maintained in a room with restricted access to pharmacy personnel only.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ENTR-601-44

Primary outcome(s)
1. Incidence and severity of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) at Day 1 to end of study
2. Incidence of abnormalities in laboratory parameters, electrocardiogram (ECG) parameters, vital sign measurements, and physical examinations at Day 1 to end of study

Key secondary outcome(s)
1. Plasma PK of ENTR-601-44 and PMO-0235a including but not limited to: maximum concentration (Cmax,) area under the curve (AUClast), and the half-life (t½) at Day 1 to end of study
2. Amounts of ENTR-601-44 and PMO-0235a excreted in urine at Day 1 to end of study

Completion date
10/06/2024

Eligibility

Key inclusion criteria
1. Male participants aged 18 to 55 years, inclusive, at Screening.
2. Body mass index (BMI) within the range of 18.0 to 32.0 kg/m², inclusive, and a minimum weight of 50.0 kg at Screening.
3. Healthy, in the opinion of the Investigator, based on medical history, physical examination, vital signs, and 12-lead ECG at Screening.
4. Clinical laboratory test results within the laboratory reference range at Screening; or, if out of range, were not clinically relevant and were acceptable to the Investigator.
5. Negative for drugs of abuse and alcohol tests at Screening and at admission on Day -1.
6. Participants with female partners who are of childbearing-potential must agree to use a highly effective method of contraception (e.g., hormonal contraception) for the duration of the study.
7. Participants able to speak, understand, read, and write English fluently to understand the nature of the study, provide written informed consent, and allow for the completion of all study assessments.
8. Capable of giving signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in the protocol.
9. Participants willing and able to abide by all study requirements and restrictions.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Male

Total final enrolment
32

Key exclusion criteria
1. Current or prior history of any of the following:
a. Any illness or medical disorder or currently under evaluation for an illness or medical disorder.
b. Difficulty with blood collection and/or poor venous access for the purposes of phlebotomy.
c. History of solid organ transplantation.
d. Malignancy within the 5 years prior to Screening with the exception of specific cancers that are cured by surgical resection (e.g., basal cell skin cancer). Participants under evaluation for possible malignancy are not eligible.
e. History of significant drug allergy, such as anaphylaxis.

f. History of renal disease, including recurrent urinary tract infections.
g. Any personal or first-degree family history of genetic kidney disease.
2. Screening ECG with clinically significant abnormalities (arrhythmias, PR > 220 msec, QRS complex > 120 msec, QT interval corrected for heart rate using Fridericia's method [QTcF] > 450 msec).
a. If the ECG is out of range, the Investigator may obtain 2 additional triplicate readings, so that up to 3 consecutive assessments are made. If the ECG data are out of range at each of these 3 consecutive assessments or based on the mean of the 3 readings, the participant is not eligible for study participation.
3. Known family history or known presence of long QT syndrome.
4. Clinically relevant hypertension (systolic blood pressure [BP] > 140 mmHg and/or diastolic BP > 90 mmHg, and heart rate > 100 bpm) at the time of Screening.
a. BP may be repeated as a triplicate up to 2 additional times. If individual values are outside the reference range at each of these 3 consecutive assessments or based on the mean of the 3 readings, the participant is not eligible for study participation.
5. eGFR <90 mL/min/1.73 m2 based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Cystatin C Equation at the time of Screening.
6. Clinical diagnosis of diabetes (glycated hemoglobin [HbA1c] > 6.5%) at the time of Screening.
7. Positive for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibody, or human immunodeficiency virus (HIV)-1 and -2 tests at Screening.
8. A positive COVID-19 test at the time of Screening or Day -1.
9. Participants receiving any prescription, over-the-counter, or herbal medications in the 14 days prior to Day -1.
10. Participants who have received any agents with nephrotoxic potential in the 30 days prior to Day -1.
11. Participants that used an investigational drug in any clinical trial within 30 days or 5 half-lives, whichever is longer, of Day 1.
12. Participants that have previously received exon skipping therapy.
13. Participants with prolonged coagulation times at the time of Screening, and/or participants with any contraindications to needle muscle biopsy, including history of keloid scarring, bleeding disorders, use of anticoagulants, or routine use of aspirin per the Investigator's discretion.

Date of first enrolment
23/08/2023

Date of final enrolment
07/05/2024

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
Entrada Therapeutics, Inc.

Funder(s)

Funder type
Industry

Funder Name
Entrada Therapeutics, Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		14/05/2025	06/06/2025	No	No
HRA research summary			20/09/2023	No	No