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A study in healthy volunteers to compare two different shaped Tiratricol tablets dissolved in water and to look at the effect of food on different doses of one shape of Tiratricol tablet

Submission date
21/04/2023

Recruitment status
No longer recruiting

Registration date
25/04/2023

Overall study status
Completed

Last Edited
11/09/2024

Condition category
Other

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The Sponsor is developing a new tablet shape (oblong) for the test medicine, Tiratricol, to treat Monocarboxylate Transporter 8 (MCT80 deficiency, also referred to as Allan-Herndon-Dudley Syndrome (AHDS). This is an ultra-rare genetic disorder which causes problems with brain development and the activity of thyroid hormones. Current treatments are limited, and the condition has a significant impact on the quality of life and overall life expectancy. This healthy volunteer study is comparing the performance of the oblong tablet against a round tablet. It is also looking to assess the safety and tolerability of the test medicine and at the effect of food and different doses using the oblong tablet.

Who can participate?
Healthy male volunteers aged 18 to 55 years.

What does the study involve?
The study consists of one part, with 5 study periods, involving a single cohort of 30 volunteers (with an optional second cohort of 15 volunteers). Volunteers receive 5 oral doses of the test medicine. All volunteers receive 350 µg (round tablet) and 350 µg (oblong tablet), both fasted, and 3 of the following 4 options: 175 µg (round tablet) or 1050 µg (round tablet), both either fed or fasted. Volunteers enter the clinical unit on Day-1 of Period 1 (the day before their first dose) and are discharged on Day 4 of Period 5 (3 days after their final dose). There is a minimum washout period of 3 days between each administration of test medicine. Volunteers complete a follow up visit 5 to 7 days after their final dose. Volunteer's blood and urine will be taken throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for approx. 7 weeks from screening to the follow up visit.

What are the possible risks and benefits of participating?
Participants get no medical benefit from taking part in the study. However, development of a treatment for MCT8 deficiency (AHDS) may benefit the population as a whole. It is considered

that the risk/benefit evaluation in this study supports the use of healthy volunteers. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Rare Thyroid Therapeutics International AB (Sweden)

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

Who is funding the study?
Rare Thyroid Therapeutics International AB (Sweden)

Who is the main contact?
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Additional identifiers

Integrated Research Application System (IRAS)
1007208

Protocol serial number
Sponsor code MCT8-2023-5

Study information

Scientific Title
Bioequivalence of two tiratricol tablets and relative bioavailability of tiratricol in the fasted and fed state in healthy male subjects combined with an assessment of dose-proportionality: a randomised, five-period crossover study

Study objectives
The trial will meet the following primary and secondary objectives:

Primary objective:
To establish bioequivalence between 350 µg Emcitate oblong tablets and 350 µg Emcitate round tablets in a fasted state (both administered as single oral doses of 1 × 350 µg tablet dispersed in water).

Secondary objectives:
1. To estimate the relative bioavailability of 1050 µg Emcitate oblong tablets in a fed state vs 1050 µg Emcitate oblong tablets in a fasted state (both administered as single oral doses of 3 × 350 µg tablets dispersed in water).
2. To estimate the relative bioavailability of 175 µg Emcitate oblong tablets in a fed state vs 175 µg Emcitate oblong tablets in a fasted state (both administered as single oral doses of 0.5 × 350 µg tablet dispersed in water).
3. To assess the dose-proportionality of Emcitate oblong tablets in a fasted state (administered as single oral doses of 175 µg [0.5 × 350 µg tablet], 350 µg [1 × 350 µg tablet] and 1050 µg [3 × 350 µg tablets] dispersed in water).
4. To further characterise the pharmacokinetics (PK) of Emcitate round tablets in a fasted state (350 µg [1 × 350 µg tablet] dose), Emcitate oblong tablets in a fasted state (175 µg [0.5 × 350 µg tablet], 350 µg [1 × 350 µg tablet], and 1050 µg [3 × 350 µg tablets] doses) and Emcitate oblong tablets in a fed state (175 µg [0.5 × 350 µg tablet] and 1050 µg [3 × 350 µg tablets] doses).

5. To provide further information on the safety and tolerability of Emcitate oblong tablets and Emcitate round tablets following oral administration.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/06/2023, London Harrow REC (Skipton House, 80 London Road, London, SE1 6LH, United Kingdom; +44 (0)207 104 8154; harrow.rec@hra.nhs.uk), ref: 23/LO/0222

Primary study design
Interventional

Study design
Single-centre randomized five-period crossover study

Study type(s)
Other

Health condition(s) or problem(s) studied
Monocarboxylate Transporter 8 (MCT8) deficiency also known as Allan Herndon Dudley Syndrome (AHDS)

Interventions
Each participant will receive a single oral dose of each of treatments A and B, and three other treatments (i.e. 5 of the 6 treatments in total) on one occasion across five study periods with a minimum 3-day washout between each period:
A. 350 µg Emicate® (Tiratricol) round tablet, fasted
B. 350 µg Emicate® (Tiratricol) oblong tablet, fasted
C. 1050 µg Emicate® (Tiratricol) oblong tablet, fasted
D. 1050 µg Emicate® (Tiratricol) oblong tablet, fed
E. 175 µg Emicate® (Tiratricol) oblong tablet, fasted
F. 175 µg Emicate® (Tiratricol) oblong tablet, fed

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Emicate® (Tiratricol)

Primary outcome(s)
PK parameters Cmax, AUC(0-last) and AUC(0-inf) for tiratricol in serum measured using blood samples at pre-dose and multiple timepoints up to 72 h post-dose

Key secondary outcome(s)
1. PK parameters, including (but not limited to): Cmax, AUC(0-last), AUC(0-inf) Tmax, T1/2, CL/F and Vz/F for tiratricol in serum, and concentration vs time profiles for serum (triiodothyronine) T3 and (thyroxine) T4 measured using blood samples at pre-dose and multiple timepoints up to

72 h post-dose
2. Incidence of adverse events (AEs), physical examinations and change from baseline for vital signs, electrocardiograms (ECGs), and laboratory safety tests (including free thyroxine [FT4], T4 and thyroid-stimulating hormone [TSH]), from the time of signing the informed consent form up until the follow-up visit (5 to 7 days post-final dose)

Completion date
31/08/2023

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study
3. Aged 18 to 55 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements
5. Healthy males
6. Body mass index (BMI) of 18.0 to 32.0 kg/m2 as measured at screening
7. Weight 50 to 100 kg at screening

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
30

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients, including lactose or galactose intolerance
2. Presence or history of any malabsorption of galactose or glucose
3. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
4. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or GI disease, neurological or psychiatric disorder, or surgical procedure or any other condition known to interfere with the absorption, distribution, metabolism, or excretion of

drugs, as judged by the investigator
5. Acute illness, surgical procedures, or trauma from within 14 days before screening (i.e. signing the ICF) until first administration of IMP, as judged by the investigator
6. History of active malignancy or neoplastic disease in the previous 12 months
7. Presence of a suspected/manifested clinically significant acute or chronic infection, as judged by the investigator
8. History of human immunodeficiency virus infection (HIV), hepatitis B, or hepatitis C; history of positive testing for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibody, or hepatitis C virus antibody (HCV Ab)
9. Subjects with a history of cholecystectomy or gallstones
10. Planned inpatient surgery, dental procedure, or hospitalisation during the study
11. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
12. Any clinically significant abnormalities in physical examination, as judged by the investigator
13. Clinically significant abnormal clinical chemistry, haematology, or urinalysis as judged by the investigator. Note: Subjects with Gilbert's Syndrome are not allowed
14. Values outside the normal reference range for any of the following safety laboratory analytes: serum TSH, T3, T4, FT4, total cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, ferritin, parathyroid hormone (PTH) or sex hormone binding globulin (SHBG,) if judged by the investigator to be clinically significant at the screening visit
15. Positive HBsAg, HCV Ab or HIV 1 and 2 antibody results at screening
16. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <80 mL/min/1.73 m2 using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI; 2009) equation
17. Any clinically significant abnormalities in vital signs (e.g. sustained [i.e. at three consecutive occasions of assessments] supine systolic blood pressure >140 mmHg, supine diastolic blood pressure >90 mmHg, or heart rate ≤35 or ≥100 beats per minute), as judged by the investigator at screening or pre dose of Period 1
18. Any clinically important abnormalities in rhythm, conduction, or morphology of resting ECG, as judged by the investigator at screening or pre dose of Period 1
19. Subjects who have received any IMP in a clinical research study within the 90 days prior to Period 1 Day 1, or less than 5 elimination half-lives prior to Period 1 Day 1, whichever is longer
20. Donation of blood or plasma within the previous 1 month or loss of greater than 400 mL of blood within the previous 3 months
21. Subjects who are taking, or have taken, any prescribed or over-the-counter drug (including anticoagulants), vitamins, dietary supplements or herbal remedies (other than up to 4 g of paracetamol per day) in the 30 days before first administration of IMP. COVID-19 vaccines are accepted concomitant medications up to 3 days before the first IMP administration and live/live-attenuated vaccines are accepted concomitant medications up to 30 days before the first IMP administration. Exceptions may apply, as determined by the investigator, if each of the following criteria are met: medication with a short half-life if the washout is such that no pharmacodynamic activity is expected by the time of first administration of IMP; and if the use of medication does not jeopardise the safety of the trial subject; and if the use of medication is not considered to interfere with the objectives of the study
22. Subjects who have had a COVID-19 vaccine within 3 days before the first IMP administration
23. Subjects who have received a live or live-attenuated vaccine within 30 days prior to the first administration of IMP
24. History of any drug or alcohol abuse in the past 2 years
25. Regular alcohol consumption in males >21 units per week (1 unit = ½ pint beer, or a 25 mL shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on type)
26. A confirmed positive alcohol breath test at screening or admission
27. Current smokers and those who have smoked within the last 12 months

28. A confirmed positive screen for urine cotinine (nicotine level above 400 ng/mL) at screening or admission
29. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
30. Confirmed positive drugs of abuse test result at screening or admission
31. Male subjects with pregnant or lactating partners
32. Subjects who are, or are immediate family members of, a study site or sponsor employee
33. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
06/07/2023

Date of final enrolment
31/08/2023

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
Rare Thyroid Therapeutics International AB

Funder(s)

Funder type
Industry

Funder Name
Rare Thyroid Therapeutics International AB

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?
HRA research summary			11/09/2024	No	No