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A study in healthy subjects to see the effects of the test medicine on the body when given in fed or fasted state as a multiple dose

Submission date 29/07/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 25/08/2022	**Overall study status** Completed	
Last Edited 17/11/2023	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
The Sponsor is developing an investigational test medicine (Acoramidis or AG10), for the potential treatment of a disease called Transthyretin amyloidosis (ATTR). ATTR is a rare but progressive disease where normally healthy proteins which carry hormones and vitamins in the blood change shape and collect in the heart, nerves and other organs, causing damage that gets worse over time and can lead to heart attacks, organ failure, and death.
The test medicine is currently being studied as a tablet to take twice daily. This trial will look at developing a new formulation (recipe) of the test medicine, which releases the medicine slowly over time, reducing the number of occasions a patient would need to take in a day.
In this trial we will look at the effects of a new formulation of the test medicine on the body and will also look at the safety and tolerability of the test medicine when administered once daily for 7 days. We may assess an alternative dose level, or the effect of food on the test medicine in Cohort 2 which is optional.

Who can participate?
This trial will take place at one non-NHS site, enrolling up to 28 male and female volunteers aged between 18 and 65.

What does the study involve?
Volunteers will receive oral doses of acoramidis MR tablet 1100 mg once daily for 7 days (Days 1 to 7) in the fasted state in Cohort 1, and in the fed state or acoramidis MR tablet XXXX mg once daily for 7 days (Days 1 to 7) in the fed or fasted state in Cohort 2. Volunteers will be discharged on Day 10 and will return to the clinic on Days 11, 12 and 14 for follow-up visits. The decision whether to commence with Cohort 2/Regimen B and the dose and prandial status to be used will only be made after a complete review of all data collected from Cohort 1/Regimen A.
Volunteer's blood and urine will be taken throughout the study for analysis of the test medicine and for their safety.
Each volunteer is expected to be involved in this study for approximately 10 weeks from screening to the final follow up phone call.

What are the possible benefits and risks of participating?
Benefits:
This is a healthy volunteer study. Participants will be administered acoramidis only for research purposes and it is not intended that the participants will receive any benefit from it. However, the information learned in this study may help future patients. Participants will be compensated for taking part in this research study with an inconvenience allowance.
Risks:
1. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers.
2. Female volunteers of childbearing potential: A fertility and early embryonic development study has been completed in rats, showing no test medicine related effects on mating and fertility in either sex or early embryonic survival. Nonclinical reproductive toxicity studies have not been completed; therefore, the test medicine should not be administered to pregnant and lactating women. Pregnant and lactating women are excluded from this clinical study. Female volunteers of childbearing potential who engage in heterosexual intercourse can only take part if they comply with the contraception requirements.
3. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation.
4. Volunteers may experience side effects from the test medicine in this study. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form(s).
When investigating new medicines there is also a risk of unexpected side effects and occasionally allergic reactions. All volunteers will be closely monitored during the study and safety assessments will be performed at regular intervals. Risks are further mitigated by ensuring that only volunteers who meet all inclusion/exclusion criteria are included and that if the safety of any volunteer represents a concern they will be withdrawn.
5. There will be an extended period of fasting for the volunteers taking part in this study. On fasted dosing volunteers will not be allowed to eat or drink anything other than water for a minimum of 10 hours, until 4 hours after each dosing at which time lunch will be provided. To ensure an adequate fluid intake, the volunteers will be monitored for signs of dehydration and fatigue. Volunteers will be provided with 240 mL of water at dosing. Volunteers will be allowed water up to 1 hour before the scheduled dosing time and will be provided with 240 mL of water at 1 hour postdose on Days 1 and 7. Water will be allowed ad libitum from 1 hour after each dose.
6. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks.
7. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.

Where is the study run from?
Quotient Sciences (UK)

When is the study starting and how long is it expected to run for?
June 2022 to August 2023

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

Who is the main contact?
medinfo@eidostx.com

Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1005767

Protocol serial number
AG10-009, QSC206655

Study information

Scientific Title
A multiple dose study to evaluate the pharmacokinetics of an acoramidis (AG10) modified release tablet formulation in healthy subjects

Study objectives
Primary objective:
To characterise the pharmacokinetics (PK- what the body does to the drug) of acoramidis (AG10) and the metabolite acoramidis-acyl glucuronide (acoramidis-AG) following multiple dose administration of an acoramidis modified release (MR) tablet formulation (recipe) in the fasted state.

Secondary objectives:
1. To characterise the PK of acoramidis (AG10) and the metabolite acoramidis-acyl glucuronide (acoramidis-AG) following multiple dose administration of acoramidis modified release (MR) tablet formulation (recipe) in the fed state (optional).
2. To determine the relative bioavailability (the proportion of test medicine that enters the body compared in two forms) of an acoramidis MR tablet formulation in the fed vs fasted state (fed state optional)
3. To characterise the PK of acoramidis (AG10) and the metabolite acoramidis-AG following multiple-dose administration of an alternative dose of acoramidis MR tablet formulation (recipe) in the fasted or fed state (optional).
4. To determine the dose linearity of an acoramidis MR tablet formulation at an alternative dose level (optional)
5. To provide additional safety and tolerability information for an acoramidis MR tablet formulation

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/08/2022, HSC REC A Office for Research Ethics Committee Northern Ireland (ORECNI) (Business Services Organisation, Lissue Industrial Estate West, 5 Rathdown Walk, Moira Road, Lisburn, BT28 2RF, UK; +44 (0)28 9536 1400; info.orecni@hscni.net), ref: 22/NI/0106

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Transthyretin (TTR) Amyloidosis (ATTR)

Interventions
Cohort 1:
Participants will receive 1100 mg acoramidis modified release (MR) tablet (2 × 550 mg tablets) once daily orally on Days 1 to 7 in the fasted state.

Cohort 2 (optional)
Participants will receive either receive 1100 mg acoramidis MR tablet (2 × 550 mg tablets) once daily orally on Days 1 to 7 in the fed state or an alternative dose of acoramidis MR tablet(s) once daily on Days 1 to 7 in the fed or fasted state.

For both cohorts, participants will return on Days 11, 12 and 14 for return visits and a follow-up phone call will take place between 30 and 34 days post-final dose to ensure the ongoing wellbeing of the subjects.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Acoramidis Modified release prototype tablets

Primary outcome(s)
1. Measurement of the PK parameters of acoramidis (AG10) and acoramidis-AG including but not limited to: Tmax, Cmax, Cmin (Day 7), Ctrough (Day 7), C24, AUC(0-tau), AUC(0-last) (Day 7), AUC (0-inf) (Day 7) and T1/2 (Day 7)
2. Assessment of dose accumulation of AG10 and acoramidis-AG for Cmax and AUC(0-tau) (Day 7 vs Day 1)

Key secondary outcome(s)
1. Measurement of the PK parameters of acoramidis (AG10) and acoramidis-AG including but not limited to: Tmax, Cmax, Cmin (Day 7), C24, AUC(0-tau), AUC(0-last) (Day 7), AUC(0-inf) (Day 7) and T1/2 (Day 7)
Assessment of dose accumulation of AG10 and acoramidis-AG for Cmax and AUC(0-tau) (Day 7 vs Day 1)
2. Assessment of the relative bioavailability for Cmax, AUC(0-tau), AUC(0-last) and AUC(0-inf), as appropriate in the fed vs fasted state
3. Measurement of the PK parameters of AG10 and acoramidis-AG including but not limited to: Tmax, Cmax, Cmin (Day 7), C24, AUC(0-tau), AUC(0-last), AUC(0-inf) (Day 7) and T1/2
4. Assessment of dose accumulation of AG10 and acoramidis-AG for Cmax and AUC (0-tau) (Day 7 vs Day 1)
5. Assessment of dose corrected PK parameters Cmax, AUC(0-tau), AUC(0-last) and AUC(0-inf), as appropriate at XX mg in the fasted state vs
1100 mg in the fasted state
6. Assessment of incidence of adverse events (AEs), physical examinations, vital signs, electrocardiograms (ECGs), and laboratory safety tests

Completion date
04/08/2023

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in one cohort
3. Aged 18 to 65 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements

5. Healthy males or non-pregnant, non-lactating healthy females
6. Body mass index (BMI) of 18.0 to 32.0 kg/m² as measured at screening
7. Body weight >50 kg at screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients
2. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
3. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator
4. Subjects with a history of cholecystectomy or gall stones
5. Subjects who do not have suitable veins for multiple venepunctures/cannulations as assessed by the investigator or delegate at screening
6. Evidence of current SARS-CoV-2 infection within 2 weeks of first IMP administration
7. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator (laboratory parameters are listed in the clinical study protocol). Subjects with Gilbert's Syndrome are allowed
8. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
9. Females of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative serum pregnancy test at screening and a negative highly sensitive urine pregnancy test at each admission)
10. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer. Subjects enrolled in Cohort 1 will not be permitted to enrol in Cohort 2. Subjects who have received acoramidis in the previous Quotient Sciences study QSC204480 (AG10-009) are permitted to take part
11. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
12. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or herbal remedies (other than up to 4 g of paracetamol per day or HRT/hormonal contraception) in the 14 days before IMP administration. COVID-19 vaccines are accepted concomitant medications. Exceptions may apply on a case by case basis, if considered not to interfere with the objectives of the study, as determined by the investigator
13. History of any drug or alcohol abuse in the past 2 years
14. Regular alcohol consumption in males >21 units per week and females >14 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)
15. A confirmed positive alcohol breath test at screening or admission
16. Current smokers and those who have smoked within the last 12 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
17. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
18. Confirmed positive drugs of abuse test result (drugs of abuse tests are listed in the clinical study protocol)
19. Male subjects with pregnant or lactating partners
20. Subjects who are, or are immediate family members of, a study site or Sponsor employee
21. Failure to satisfy the investigator of fitness to participate for any other reason
22. In the judgment of the investigator or Sponsor, has any clinically important ongoing medical condition or laboratory abnormality or other condition that might jeopardise the subject's safety, increase their risk from participation, or interfere with the study

Date of first enrolment
30/08/2022

Date of final enrolment
22/10/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Eidos Therapeutics, Inc.

Funder(s)

Funder type
Industry

Funder Name
Eidos Therapeutics, Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to confidentiality.

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			28/06/2023	No	No