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A healthy volunteer study to asses the safety, tolerability and blood levels of AUT00206 tablets

Submission date
24/09/2021

Recruitment status
No longer recruiting

Registration date
28/09/2021

Overall study status
Completed

Last Edited
10/12/2024

Condition category
Other

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

Plain English summary of protocol

Background and study aims
This is a study of AUT00206 (the study medicine), an experimental new medicine with the potential to treat Fragile X syndrome. We're doing this study to find out the blood levels and side effects of the study medicine in healthy volunteers (both men and women).

Background of the disease: Fragile X syndrome (FXS) is the most common inherited cause of learning disability, affecting about 1 in 7000 boys and men, and 1 in 11,000 girls and women. It causes a wide range of problems with learning and behaviour. Currently, there are no medicines that specifically treat FXS. AUT00206 (the study medicine) is an experimental new medicine for treating FXS. It acts at sites on nerve cells (called voltage-gated potassium channels) that help to control electrical signalling in parts of the brain involved in learning and behaviour. So, we hope it will be a useful treatment for FXS.

Who can participate?
Healthy male and female volunteers aged 18 – 45 years.

What does the study involve?
The study will be in 3 parts (Parts A1, A2 and B). During the 4 weeks before the study potential subjects will have a screening visit, to see if they are suitable.
In Part A1 there are 4 study sessions and it takes about 11 weeks to complete the study, from first admission to the ward in Session 1 until final follow up visit (after Session 4). In Part A2 there may be 1 or 2 study sessions and it will take about 6 weeks to complete the study.
In each study session subjects will:
-Take a dose of study medicine or placebo (a dummy medicine that looks the same as the study medicine but has no active ingredient) by mouth, as either a single dose in the morning; or 2 single doses – one dose in the morning and one in the evening
-Give many samples of your blood
-Have numerous safety assessments done
-Stay on the ward for 3 nights in a row and make 4 outpatient visits
Subjects will have a final follow-up visit about 2 weeks after the last dose of study medicine.

What are the possible benefits and risks of participating?
There is no medical benefit from taking part in the study. To date 91 people have taken a capsule form of the study medicine and there were no important side effects. Some people had headache, drowsiness, abdominal pain, or nausea. The study medicine has also been thoroughly tested in laboratory animals, and there were no concerns for testing the study medicine in humans. Some animals had small increases in liver and thyroid weight, which returned to normal after treatment stopped. We'll do blood tests during the study to monitor subjects liver and thyroid.
As with any new medicine that only a few people have taken, we don't yet know all its side effects.

Where is the study run from?
Hammersmith Medicines Research (UK)

When is the study starting and how long is it expected to run for?
June 2021 to April 2022

Who is funding the study?
Autifony Therapeutics Limited (UK)

Who is the main contact?
hmr@hmrlondon.com
Alice.Sharman@autifony.com

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003211-26

Integrated Research Application System (IRAS)
1003888

Protocol serial number

AUT041206

Study information

Scientific Title
A randomised, double-blind, placebo-controlled, single and repeated dose escalation study to assess the safety, tolerability, pharmacokinetics and food effect of a new formulation of AUT00206 in healthy men and women

Study objectives
A tablet formulation of AUT00206 has been developed with the intention of reducing the food effect and increasing the absorption of AUT00206 when compared with the AUT00206 capsule which was previously developed by Autifony. The present trial will be the first administration of the tablet formulation to humans, and will assess the safety, tolerability, and PK (including food effect) of single and repeated doses of the of the AUT00206 tablet formulation in healthy men and women

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/08/2021, Fast Track REC (no address available; no telephone number available; fasttrack.rec@hra.nhs.uk), ref: 21/FT/0094

Primary study design
Interventional

Study design
Phase 1 single-centre placebo-controlled double-blinded randomized interventional study

Study type(s)
Other

Health condition(s) or problem(s) studied
Phase 1 study in healthy volunteers of a treatment to improve and/or normalize symptoms and deficits in patients with Fragile X Syndrome (FXS)

Interventions
Current intervention as of 21/01/2022:
Part A1: Single Ascending Dose, cross-over design; subjects will be dosed in up to 4 sessions.
Group 1 males - 6 subjects AUT00206 active; 2 subjects placebo to match
Group 2 males - 6 subjects AUT00206 active; 2 subjects placebo to match
Optional Part A2: Single Ascending Dose. Cross-over design; subjects will be dosed in up to 2 sessions.
Group 1 females - 6 subjects AUT00206 active; 2 subjects placebo to match

Optional PART B: Multiple Ascending Dose (7 - 10 days, based on predicted time to steady state)
Group 1 - 6 subjects AUT00206 active; 2 placebo

Group 2 - 6 subjects AUT00206 active; 2 placebo
Group 3 - 6 subjects AUT00206 active; 2 placebo
Group 4 - 6 subjects AUT00206 active; 2 placebo

All subjects will be dosed orally. Whether subjects receive either a single dose or 2 single doses (one in the morning and one in the evening) of AUT00206 or placebo, and whether the dose is taken fed or fasted, will be determined based on the pharmacokinetic data as it becomes available.

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Group 3 - 6 subjects AUT00206 active; 2 placebo
Group 4 - 6 subjects AUT00206 active; 2 placebo

All subjects will be dosed orally. Whether subjects receive either a single dose or 2 single doses (one in the morning and one in the evening) of AUT00206 or placebo, and whether the dose is taken fed or fasted, will be determined based on the pharmacokinetic data as it becomes available.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
AUT00206

Primary outcome(s)
Part A1:
1.1 Pharmacokinetic (PK) profile of AUT00206 after single oral doses of AUT00206 in healthy men measured from blood samples taken before and frequently after dosing up to 192h
1.2 Effect of food on the bioavailability of single oral doses of AUT00206 in healthy men measured from blood samples taken before and frequently after dosing

Part A2 (optional):
2. PK profile of AUT00206 after single oral doses of AUT00206 in healthy women measured from blood samples taken before and frequently after dosing up to 192h

Part B (optional):
3. PK profile of AUT00206 after repeated oral doses of AUT00206 in healthy men measured from blood samples taken before and frequently after dosing up to 192h

Key secondary outcome(s)
Part A1:
1. Safety and tolerability of single oral doses of AUT00206 in healthy men measured by collecting vital signs (blood pressure, heart rate, tympanic temperature, and respiratory rate), 12-lead electrocardiogram (ECG)s, physical examinations, and laboratory safety tests (haematology, clinical chemistry, thyroid function, and urinalysis), at frequent intervals; the Columbia-Suicide Severity Rating Scale (C-SSRS) will be conducted at Screening and follow-up, and collecting reports of adverse events (AEs) throughout the study

Part A2 (optional):
2. Safety and tolerability of single oral doses of AUT00206 in healthy women measured by collecting vital signs (blood pressure, heart rate, tympanic temperature, and respiratory rate), 12-lead electrocardiogram (ECG)s, physical examinations, and laboratory safety tests (haematology, clinical chemistry, thyroid function, and urinalysis), at frequent intervals; the Columbia-Suicide Severity Rating Scale (C-SSRS) will be conducted at Screening and follow-up, and collecting reports of adverse events (AEs) throughout the study

Part B (optional):
3. To assess the safety and tolerability of repeated oral doses of AUT00206 in healthy men measured by collecting vital signs (blood pressure, heart rate, tympanic temperature, and respiratory rate), 12-lead electrocardiogram (ECG)s, physical examinations, and laboratory safety tests (haematology, clinical chemistry, thyroid function, and urinalysis), at frequent intervals; the Columbia-Suicide Severity Rating Scale (C-SSRS) will be conducted at Screening and follow-up, and collecting reports of adverse events (AEs) throughout the study

Completion date
12/04/2022

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 21/01/2022:
1. Healthy male volunteer (Parts A1 and B only) or healthy female volunteer (Part A2 only).
2. Aged 18 - 45 years (at [first] dosing) (Part A and Part B Groups 1 and 2) or aged >18 years and targeted towards those aged >45 years (Part B Groups 3 and 4)
3. A BMI (Quetelet index) in the range 18.0 - 31.0 kg/m²
4. Sufficient intelligence to understand the nature of the trial and any hazards of participating in it. Ability to communicate satisfactorily with the investigator and to participate in, and comply with the requirements of, the entire trial.
5. Willingness to give written consent to participate after reading the information and consent form, and after having the opportunity to discuss the trial with the investigator or their delegate.
6. Agree to follow the contraception requirements of the trial as described in the protocol/ICF.
7. Agree not to donate blood or blood products during the study and for up to 3 months after the administration of the trial medication.
8. Willingness to give written consent to have data entered into The Overvolunteering Prevention System (TOPS).

Previous participant inclusion criteria:
1. Healthy male volunteer (Parts A1 and B only) or healthy female volunteer (Part A2 only).
2. Aged 18 - 45 years (at [first] dosing).
3. A BMI (Quetelet index) in the range 18.0 - 31.0 kg/m²

4. Sufficient intelligence to understand the nature of the trial and any hazards of participating in it. Ability to communicate satisfactorily with the investigator and to participate in, and comply with the requirements of, the entire trial.
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Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
41

Key exclusion criteria
1. Woman who is pregnant or lactating, or pre-menopausal woman who is sexually active and not using a highly-effective method of contraception.
2. Clinically relevant abnormal history, physical findings, ECG, or laboratory values at the pre-trial screening assessment that could interfere with the objectives of the trial or the safety of the volunteer.
3. Presence of acute or chronic illness or history of chronic illness sufficient to invalidate the volunteer's participation in the trial or make it unnecessarily hazardous.
4. Impaired endocrine, thyroid, hepatic, respiratory or renal function, diabetes mellitus, coronary heart disease, post-COVID-19 syndrome ('long COVID'), or history of any psychotic mental illness.
5. Surgery (eg stomach bypass) or medical condition that might affect absorption of medicines.
6. Presence or history of severe adverse reaction to any drug, or a history of sensitivity to AUT00206 or its excipients.
7. Use of a prescription medicine (except oral contraceptives in females) during the 30 days before the first dose of trial medication, or use of an over-the-counter medicine, with the exception of acetaminophen (paracetamol), during the 7 days before the first dose of trial medication.
8. Use of vaccine (including COVID-19 vaccine) during the 7 days, before first receipt of trial medication until the end of the study.
9. History of epilepsy or seizures.
10. Receipt of an investigational product (including prescription medicines) as part of another clinical trial within the 3 months before [first] admission to this study; in the follow-up period of

another clinical trial at the time of screening for this study.
11. Presence or history of drug or alcohol abuse, or intake of more than 14 units of alcohol weekly.
12. Smoking of more than 5 cigarettes daily.
13. Blood pressure and heart rate in supine position at the screening examination outside the ranges: blood pressure 90–140 mm Hg systolic, 40–90 mm Hg diastolic; heart rate 40–100 beats /min.
14. QT value, measured at screening visit, greater than 450 msec (men) or 470 msec (women) on 12-lead ECG, using Fridericia's formula (QTcF) for correction.
15. Alanine aminotransferase (AST), aspartate aminotransferase (ALT) or alkaline phosphatase (AP) ≥ 1.5 x the upper limit of normal (ULN). A repeat is allowed on one occasion for determination of eligibility.
16. Possibility that the volunteer will not cooperate with the requirements of the protocol.
17. Positive test for hepatitis B, hepatitis C or HIV consistent with ongoing infection.
18. Vegans or people who are on a restricted diet for medical reasons (eg lactose intolerant); or unwilling to eat a high-fat breakfast (Part A1 and A2 only).
19. Positive result for suicidal ideation or behaviour using the C-SSRS, including a positive response to items 3 to 5; or a history of suicidal behaviour in the past year
20. Loss of more than 400 mL blood during the 3 months before the trial, eg as a blood donor.
21. Medical objection by General Practitioner (GP) to volunteer entering trial.

Date of first enrolment
01/09/2021

Date of final enrolment
12/04/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Hammersmith Medicines Research
Cumberland Ave
London
United Kingdom
NW10 7EW

Sponsor information

Organisation
Autifony Therapeutics (United Kingdom)

ROR
https://ror.org/005mj6e76

Funder(s)

Funder type
Industry

Funder Name
Autifony Therapeutics Ltd

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Funder report results	version 1	04/10/2022	14/11/2022	No	No