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A trial to evaluate the safety, tolerability, and pharmacokinetics of AQ280 in healthy subjects

Submission date
30/04/2022

Recruitment status
No longer recruiting

Registration date
08/07/2022

Overall study status
Completed

Last Edited
06/04/2023

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
AQ280 belongs to a class of drugs known as highly selective JAK-1 inhibitors. JAK-1 inhibitors interrupt the inflammatory pathway in the body. It is hoped that AQ280 will be an effective new treatment for a condition called eosinophilic oesophagitis, a chronic, allergic inflammatory condition of the oesophagus (the tube connecting the mouth to the stomach).

Who can participate?
Healthy volunteers aged 18 to 65 years.

What does the study involve?
Part A will comprise a single dose, sequential group, escalating-dose design; also incorporating a single group, 2 period crossover arm investigating the effect of dosing AQ280 with food compared to dosing whilst fasting. Approximately 40 participants are planned to be studied in 5 cohorts (Cohorts A1 to A5; with one of the cohorts including the food-effect evaluation). In each cohort, 6 participants will receive AQ280 and 2 participants will receive placebo. Each participant will reside at the study site from Day -1 to Day 3 of the treatment period and a safety follow-up phone call will be conducted 1 week after dosing. The Day 1 dose will be administered in the fasted state in all cohorts except for treatment period 2 of the food effect cohort where it will be administered after eating a high fat breakfast.

Part B will comprise a multiple dose, sequential group, escalating-dose design. Approximately 24 participants are planned to be studied in 3 cohorts (Cohorts B1 to B3). In each cohort, 6 participants will receive AQ280 and 2 participants will receive placebo. Each participant will reside at the study site from Day -1 to Day 9. Dosing is planned to be once daily on Days 1 to 7 and a safety follow-up visit will be conducted 1 week after the final dose.

The total duration of study participation for each participant is anticipated to be approximately 6 weeks (8 weeks for the food effect cohort) in Part A and 7 weeks in Part B.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration

Risks:
The starting dose has been selected based on the preclinical data with the intention that it will be a safe and well tolerated starting dose. Strict dose escalation stopping criteria will apply during the study to minimise the risk to study participants, these are based on the effects seen in animal studies as well as the side effects seen with other drugs within the same class.

Participants will be closely monitored whilst on the clinical trial for potential drug effects (eg. adverse events (particularly infections), laboratory value changes (particularly evidence of anaemia, neutropenia and thrombocytopenia), vital signs or ECG changes). Any abnormalities will be followed up until resolution.

Where is the study run from?
Aqilion AB (Sweden)

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

Who is funding the study?
Aqilion AB (Sweden)

Who is the main contact?
Dr Ashley Brooks, ashley.brooks@labcorp.com

Contact information

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Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05485779

Integrated Research Application System (IRAS)
1005473

Protocol serial number
ARIA-1

Study information

Scientific Title
A randomized, double-blind, placebo-controlled, single and multiple ascending dose and food effect evaluation trial to evaluate the safety, tolerability, and pharmacokinetics of AQ280 in healthy subjects

Study objectives
• To evaluate the safety and tolerability of single and multiple ascending oral doses of AQ280, and to determine a safe therapeutic range of AQ280 in healthy subjects
• To determine the PK of AQ280 after single and multiple oral doses
• To determine the PK of the AQ280 main metabolite, AQ282, after single and multiple oral doses
• To determine the effect of food on the PK of AQ280 after single oral dose

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 06/06/2022, London Riverside Research Ethics Committee (Level 3 Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8150, +44 (0)207 104 8013; riverside.rec@hra.nhs.uk), ref: 22/FT/0063

Study design
Interventional double blind randomized single and multiple ascending dose trial with sequential groups and crossover design placebo controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Allergic reaction in the gullet

Interventions
Part A will comprise a single dose, sequential group, escalating-dose design; also incorporating a single group, 2 period crossover arm investigating the effect of dosing AQ280 with food compared to dosing whilst fasting. Approximately 40 participants are planned to be studied in 5 cohorts (Cohorts A1 to A5; with one of the cohorts including the food-effect evaluation). In each cohort, 6 participants will receive AQ280 and 2 participants will receive placebo. Each participant will reside at the study site from Day -1 to Day 3 of the treatment period and a safety follow-up phone call will be conducted 1 week after dosing. The Day 1 dose will be administered in the fasted state in all cohorts except for treatment period 2 of the food effect cohort where it will be administered after eating a high fat breakfast.

Part B will comprise a multiple dose, sequential group, escalating-dose design. Approximately 24 participants are planned to be studied in 3 cohorts (Cohorts B1 to B3). In each cohort, 6 participants will receive AQ280 and 2 participants will receive placebo. Each participant will reside at the study site from Day -1 to Day 9. Dosing is planned to be once daily on Days 1 to 7 and a safety follow-up visit will be conducted 1 week after the final dose.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
AQ280

Primary outcome(s)
1. Number of TEAEs per subject daily from signed consent to end of trial
2. Clinically significant abnormalities in vital signs (systolic and diastolic blood pressure, pulse rate, and oral body temperature) multiple timepoints per day from screening until end of trial
3. Abnormal ECG (QTcF interval of >450 msec for males and >470 msec for females, or change from baseline of >30 msec) measured from Day 1 (postdose) up until 48 hours postdose in Part A and up to the follow-up visit in Part B. Safety ECG: Part A/B: from screening and on Day 1, 3, 5, 7,8, 9

4. Clinically significant changes in laboratory evaluations on multiple days from dosing until end of trial

Key secondary outcome(s))
Part A at predose and multiple timepoints up to 48 hours postdose:
1. Primary PK parameters derived from plasma concentration-time profile of AQ280: AUC0-∞, Cmax (AUC0-t last may be included as a primary PK parameter if AUC0-∞ cannot be calculated)
2. Primary PK parameters derived from plasma concentration-time profile of the AQ280 main metabolite, AQ282: AUC0-∞, Cmax (AUC0-t last may be included as a primary PK parameter if AUC0-∞ cannot be calculated)
3. Comparison of the primary PK parameters of AQ280 after single dose administration in the fasted state and in the fed state

Part B at predose and multiple timepoints during Day 1 and Day 7, as well as daily until end of trial:
1. Primary PK parameters derived from plasma concentration-time profile of AQ280 on Day 1 and Day 7: AR, AUCτ, Cmax
2. Primary PK parameters derived from plasma concentration-time profile of the AQ280 main metabolite, AQ282, on Day 1 and Day 7: AUCτ, Cmax

Completion date
10/07/2023

Eligibility

Key inclusion criteria
1. Males or females, of any race, between 18 and 65 years of age, inclusive.
2. Body mass index between 18.0 and 32.0 kg/m², inclusive.
3. In good health, determined by no clinically significant findings from medical history, 12-lead ECG, vital sign measurements, and clinical laboratory evaluations at screening and check-in and from the physical examination at check-in, as assessed by the investigator (or designee).
4. Females will not be pregnant or lactating, and females of childbearing potential and males will agree to use contraception
5. Able to comprehend and willing to sign an ICF and to abide by the study restrictions.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal, neurological, respiratory, endocrine, or psychiatric disorder, as determined by the investigator (or designee).
2. History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, as determined by the investigator (or designee).
3. History of any surgical (eg, stomach or intestinal surgery or resection) or medical condition that would potentially alter absorption, distribution, metabolism, and/or excretion of orally administered drugs. Uncomplicated appendectomy and hernia repair will be allowed. Cholecystectomy will not be allowed.
4. History of any significant infectious disease, as assessed by the investigator, within 2 weeks prior to the first dose of IMP.
5. AST and/or ALT values >1.2 × ULN.
6. Congenital nonhemolytic hyperbilirubinaemia (including suspicion of Gilbert's syndrome).
7. Hemoglobin value, neutrophil count, and/or lymphocyte count < lower limit of normal.
8. Clinically significant abnormal ECG at screening or check-in.
9. Positive hepatitis panel and/or positive human immunodeficiency virus test. Subjects whose results are compatible with prior immunization may be included at the discretion of the investigator
10. Current active tuberculosis based on Quantiferon™ tuberculosis (TB) Gold test.

Date of first enrolment
01/07/2022

Date of final enrolment
26/06/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Aqilion AB

Funder(s)

Funder type
Industry

Funder Name
Aqilion AB

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
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No