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Comparability study of anifrolumab administered using a medical device in healthy volunteers

Submission date
10/02/2022

Recruitment status
No longer recruiting

Registration date
11/04/2022

Overall study status
Completed

Last Edited
06/03/2023

Condition category
Skin and Connective Tissue Diseases

[ ] 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 clinical trial will compare the delivery of the clinical trial medicine, a compound called Anifrolumab. Anifrolumab has been granted marketing authorization by the United States (US) Food and Drug Administration (FDA) for intravenous (IV) infusion, however, the use of an autoinjector (AI) (a type of automatic syringe) or an accessorized prefilled syringe (APFS) to deliver this clinical trial medicine has not been tested before. The participants will receive the clinical trial medicine once via AI or APFS.
The main purpose of the clinical trial is to examine the levels of the clinical trial medicine in blood after a single dosing under the skin using an AI compared to an APFS. The study will also look at how the clinical trial medicine is taken up, metabolised (chemically broken down), distributed through the body and excreted when it is injected in different places in your body (upper arm, lower abdomen, or front thigh) as well as the safety and tolerability of the clinical trial medicine when administered via AI versus APFS.

Who can participate?
Healthy male and female participants between the ages of 18 to 55 years.

What does the study involve?
The trial comprises a screening Period of up to 28 days, one in-house stay of about 3 days and 8 outpatient visits.

What are the possible benefits and risks of participating?
This study will be conducted to compare the pharmacokinetic (PK) exposure after a single SC dose of anifrolumab administered using an AI with the PK exposure after a single subcutaneous (SC) dose of anifrolumab administered using APFS in healthy male and female volunteers.

Where is the study run from?
Parexel International (UK)

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

Who is funding the study?
AstraZeneca (USA)

Who is the main contact?
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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2021-004896-14

IRAS number
1004577

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
D3465C00002, IRAS 1004577

Study information

Scientific Title
A multicenter, randomized, open-label, parallel phase 1 comparability study of anifrolumab administered using Accessorized Pre-Filled Syringe (APFS) or Autoinjector (AI) in healthy volunteers

Acronym
APFS to AI PK Bridging Study in Anifrolumab

Study objectives
1. To demonstrate that the pharmacokientic (PK) exposure following single SC administration of anifrolumab by AI is comparable to the PK exposure following single SC administration of anifrolumab using APFS.
2. To evaluate the PK of anifrolumab administered to various anatomical injection sites and in healthy subjects within different body weight ranges.
3. To evaluate the safety and tolerability of AI- vs APFS-administered anifrolumab.
4. To evaluate the immunogenicity of anifrolumab delivered by AI or APFS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, To be requested (), ref: 22/LO/0086

Study design
Interventional multicenter randomized open-label parallel comparability study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Systemic lupus erythematosus (SLE)

Interventions
After meeting the eligibility criteria, all eligible participants will be randomized 1:1:1:1:1:1 to a device group (APFS or AI) for an anatomical injection site as defined in the protocol. Randomization will be stratified by protocol defined body weight categories.

AI arm: Randomized participants will receive a single SC dose of anifrolumab via autoinjector (AI)
APFS arm: Randomized participants will receive a single SC dose of anifrolumab via accessorized pre-filled syringe (APFS)

Intervention Type
Drug

Phase
Phase I

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

Primary outcome measure
Measured using blood test from Day 1 to Day 57
1. Area under serum concentration-time curve from time zero extrapolated to infinity (AUCinf).
2. Area under serum concentration-time curve from time zero to last quantifiable concentration (AUClast).
3. Maximum observed serum (peak) drug concentration (Cmax).

Secondary outcome measures
Measured using blood test from Day 1 to Day 57
1. Time to reach peak or maximum observed concentration (tmax).
2. Half-life associated with terminal slope (λz) of a semi-logarithmic concentration-time curve (t1/2λz).
3. Mean residence time of the unchanged drug in the systemic circulation from zero to infinity (MRT).
4. Apparent total body clearance of drug after extravascular administration (CL/F).
5. Apparent volume of distribution following extravascular administration (based on terminal phase) (Vz/F).
6. Time of last quantifiable concentration (tlast).

Measured at screening period (Day -28 to Day-2) through follow-up visit (Day 57)
7. Adverse Events, Injection site pain and pruritis assessed using visual analog scale 100 mm, Injection site erythema, induration and swelling assessed using the injection site reaction score, Vital signs (systolic and diastolic blood pressure, pulse and body temperature), 12-lead Electrocardiogram, Physical examination, Laboratory assessments (hematology, clinical chemistry, and urinalysis).
8. Anti-drug antibodies (ADA) measured using ... at Day 1, 29 and 57

Overall study start date
08/02/2022

Completion date
11/04/2023

Eligibility

Key inclusion criteria
1. Healthy male and female subjects (childbearing and non-childbearing potential) aged 18 – 55 years (inclusive) at Screening with suitable veins for cannulation or repeated venipuncture at screening.
2. Female subjects of childbearing potential must have a negative pregnancy test at Screening.
3. Female subjects of childbearing and non-childbearing potential and male subjects must adhere to the contraception methods.
4. Have a body mass index between 18.5 and 30 kg/m² inclusive and weigh at least 50 kg and no more than 110 kg inclusive at Screening.
5. Subjects must have immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), either by having recovered from a SARS-CoV-2 infection (should have recovered from infection at least 6 weeks before Screening Visit as confirmed by a COVID-19 test) or fully vaccinated against SARS CoV-2 with vaccines approved in the local region (should have received the final vaccine dose at least 2 weeks before Screening Visit).
6. Subject should meet all of following tuberculosis (TB) criteria:
6.1. No signs or symptoms of active TB prior to or during any Screening visit.
6.2. No medical history or past physical examinations suggestive of active TB.
6.3. No recent contact with a person with active TB OR if there has been such contact, referral to a physician specializing in TB to undergo additional evaluation prior to randomization (documented comprehensively in source), and, if warranted, receipt of appropriate treatment for latent TB at or before the first administration of IP.
6.4. No history of latent TB prior to initial Screening visit, with the exception of latent TB with documented completion of appropriate treatment.
7. Negative result for an Interferon-gamma (IFN-γ) release assay (IGRA) (eg QuantiFERON-TB Gold [QFT-G] test) test for TB at screening.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
180

Total final enrolment
180

Key exclusion criteria
1. Lactating or pregnant females or females who intend to become pregnant or begin breastfeeding anytime from initiation of Screening until 1 month after the final Follow-up Visit.
2. History or presence of hepatic or renal diseases known to interfere with the PK of anifrolumab.

3. Any clinically significant illness, medical/surgical procedure, or trauma within 4 weeks of the administration of SI, as judged by the Investigator.
4. Any clinically significant abnormalities in in clinical chemistry, hematology, or urinalysis results, at Screening and/or admission to the Clinical Unit.
5. Any clinically significant abnormal findings in vital signs at Screening and/or admission to the Clinical Unit.
6. Any clinically significant abnormalities on 12-lead electrocardiogram at Screening and/or admission to the Clinical Unit, as judged by the Investigator.
7. Any positive result on Screening for serum hepatitis B surface antigen OR anti-HBc antibody, hepatitis C antibody, and HIV antibody.
8. Opportunistic infection requiring hospitalization or IV antimicrobial treatment within 3 years of randomization.
9. Clinically significant chronic infection (eg, osteomyelitis, bronchiectasis, etc.) within 8 weeks prior to signing the informed consent form (ICF).
10. Any infection requiring hospitalization or treatment with IV anti-infective medications not completed at least 4 weeks prior to signing the ICF.
11. Any infection requiring oral anti-infective medications (including antivirals) within 2 weeks prior to Day 1
12. History of severe Coronavirus Disease 2019 (COVID-19) infection requiring hospitalization within the last 12 months prior to Screening, or clinical history compatible with Long COVID 19 (symptoms beyond 12 weeks of acute infection), as judged by the Investigator
13. COVID-19 infection before or during Screening and/or admission confirmed by a COVID 19 test (in the London Clinical Unit, subjects will undergo COVID-19 testing prior to ICF signing and any subject testing positive will not be screened for the study).
14. Known or suspected history of drug abuse, as judged by the Investigator.
15. Positive screen for drugs of abuse or cotinine at Screening or on admission to the Clinical Unit or positive screen for alcohol at Screening or on admission to the Clinical Unit.
16. Participation in another clinical trial, or has received another new chemical entity (defined as a compound which has not been approved for marketing) within 3 months of the administration of SI in this study. The period of exclusion begins 3 months after the final dose or 5 half-lives, whichever is the longest.
17. Plasma donation within 1 month of Screening or any blood donation/loss more than 500 mL during the 3 months prior to Screening.
18. A known history of allergy or reaction to any component of the IP formulation or history of anaphylaxis to any human gamma globulin therapy.
19. Current smokers or those who have smoked or used nicotine products (including e-cigarettes) within the 3 months prior to Screening.
20. Use of drugs with enzyme-inducing properties such as St John’s Wort within 3 weeks prior to the administration of SI.
21. Known or suspected history of alcohol or drug abuse or excessive intake of alcohol as judged by the Investigator. Excessive intake of alcohol defined as the regular consumption of more than 24 g of alcohol per day for men or 12 g of alcohol per day for women (for the London unit: regularly consuming >21 units of alcohol per week for males or >14 units of alcohol per week for females).
22. Excessive intake of caffeine-containing drinks or food (eg, coffee, tea, chocolate) as judged by the Investigator. Excessive intake of caffeine defined as the regular consumption of more than 600 mg of caffeine per day (eg, >5 cups of coffee) or would likely be unable to refrain from the use of caffeine-containing beverages during confinement at the investigational site.
23. Subjects who have previously received anifrolumab.

Date of first enrolment

23/02/2022

Date of final enrolment
23/02/2023

Locations

Countries of recruitment
Germany

United Kingdom

United States of America

Study participating centre
Parexel International Limited
Northwick Park Hospital
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Study participating centre
Parexel International – EPCU Berlin
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Study participating centre
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Sponsor information

Organisation
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Sponsor type
Industry

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ROR
https://ror.org/043cec594

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/11/2023

Individual participant data (IPD) sharing plan

Coded study data will be shared via secure Sponsor systems. Data sharing will be in accordance with current data privacy legislation and restricted to authorised parties with the necessary confidentiality agreements in place

Qualified researchers can request access to anonymized individual patient-level data from AstraZeneca group of companies sponsored clinical trials via the request portal. All requests will be evaluated as per the AZ disclosure commitment: https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.
AZ are accepting requests for IPD, but this does not mean all requests will be shared.

AstraZeneca will meet or exceed data availability as per the commitments made to the EFPIA Pharma Data Sharing Principles. For details of our timelines, please refer to our disclosure commitment at: https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

When a request has been approved AstraZeneca will provide access to the de-identified individual patient level data in an approved sponsored tool. Signed Data Sharing Agreement (non-negotiable contract for data accessors) must be in place before accessing requested information. Additionally, all users will need to accept the terms and conditions of the SAS MSE to gain access. For additional details, please review the Disclosure Statements at: https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

https://astrazenecagroup-dt.pharmacm.com/DT/Home

IPD sharing plan summary

Available on request

Study outputs

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