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A study in healthy volunteers to investigate the safety and tolerability of a new test medicine (DES-9384)

Submission date
05/05/2023

Recruitment status
No longer recruiting

Registration date
09/05/2023

Overall study status
Completed

Last Edited
20/08/2026

Condition category
Other

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

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, DES-9384, for the potential treatment of rheumatoid arthritis. Rheumatoid arthritis is an autoimmune disease which occurs when the immune system attacks the cells which line the joints by mistake, making the joints swollen, stiff and painful. Over time the joints, cartilage and nearby bone can become damaged. The condition usually affects the hands, feet and wrists.

Who can participate?
Healthy male and non-pregnant, non-lactating female volunteers aged between 18 and 55 years.

What does the study involve?
In Part 1, up to 56 volunteers will be split into seven cohorts. Each cohort will receive two oral doses of the test medicine at different dose levels, or placebo, 12 hours apart and in the fasted state. Following a minimum 7-day washout period Cohort 4 only will take part in Period 2, where volunteers will receive 2 oral doses of the test medicine, or placebo, 12 hours apart in the fed state. Volunteers will be discharged 48 hours post morning dose in each study period and will return for a follow-up visit 3-5 days after discharge.
In Part 2, up to 48 volunteers will be split into four cohorts. Based on Part 1 results, each cohort will receive either one or two oral doses a day of the test medicine, or placebo, for 7 consecutive days, in the fasted state. Volunteers will be discharged 48 hours post final dose and will return for a follow-up visit 3-5 days after discharge.
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 approximately 6 weeks from screening to the follow-up visit for all cohorts in Part 1 except Cohort 4, who are expected to be involved for 7 weeks, and approximately 6 weeks for volunteers in Part 2.

What are the possible risks and benefits of participating?
Healthy volunteers will get no medical benefit from the test medicine; however, the aims of the study can be most efficiently met in volunteers with no concurrent medical conditions and who

do not need to take concomitant medication that might interfere with the study objectives or increase the risk of the study. The risk/benefit evaluation in this study supports the use of healthy volunteers.

Where is the study run from?
Quotient Sciences Limited (United Kingdom)

When is the study starting and how long is it expected to run for?
July 2023 to February 2024

Who is funding the study?
D. E. Shaw Research, LLC (USA)

Who is the main contact?
recruitment@weneedyou.co.uk

Contact information

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Principal investigator

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Integrated Research Application System (IRAS)
1007622

CRO study code
QSC300414

Study information

Scientific Title
A two-part first-in-human study to assess the safety, tolerability, pharmacokinetics and pharmacodynamic effects of single and multiple ascending oral doses of DES-9384 in healthy male and female subjects

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

Primary objectives
1. To assess the safety and tolerability of single twice daily (BID) (Part 1) and multiple once daily (QD) or BID (Part 2) ascending doses of DES-9384 administered as an oral capsule to healthy male and female subjects

Secondary objectives
1. To characterise the PK following single BID (Part 1) and multiple QD or BID (Part 2) ascending oral doses of DES-9384 administered as a capsule
2. To assess the effect of food (Part 1) on the PK of a capsule formulation of DES-9384

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 15/05/2023, Health and Social Care Research Ethics Committee B (Office for Research Ethics Committees in Northern Ireland (ORECNI), Lissue Industrial Estate West, 5 Rathdown Walk, Lisburn, BT28 2RF, United Kingdom; -; RECB@hscni.net), ref: 23/NI/0043

2. Approved 15/05/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, United Kingdom; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 57954/0001/001-0001

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Phase I study in healthy volunteers

Study type(s)
Other

Health condition(s) or problem(s) studied
Rheumatoid arthritis (RA), other inflammatory diseases, or pain

Interventions
In Part 1, up to 56 volunteers will be split into seven cohorts. Each cohort will receive two oral doses of the test medicine at different dose levels, or placebo, 12 hours apart and in the fasted state. Following a minimum 7-day washout period Cohort 4 only will take part in Period 2, where volunteers will receive 2 oral doses of the test medicine, or placebo, 12 hours apart in the fed state. Volunteers will be discharged 48 hours post morning dose in each study period and will return for a follow-up visit 3-5 days after discharge.

Cohort 1: 10 mg dose twice a day on one occasion
Cohort 2: 30 mg dose twice a day on one occasion
Cohort 3: 90 mg dose twice a day on one occasion
Cohort 4: 60 mg dose twice a day on two occasions
Cohort 5: 120 mg dose twice a day on one occasion
Cohort 6: 140 mg dose twice a day on one occasion
Cohort 7: 270 mg dose twice a day on one occasion

In Part 2, up to 48 volunteers will be split into four cohorts. Based on Part 1 results, each cohort will receive either one or two oral doses a day of the test medicine, or placebo, for 7 consecutive days, in the fasted state. Volunteers will be discharged 48 hours post final dose and will return for a follow-up visit 3-5 days after discharge.

Cohort 1: 90 mg dose twice a day for 7 consecutive days
Cohort 2: 180 mg dose twice a day for 7 consecutive days
Cohort 3: 270 mg dose twice a day for 7 consecutive days
Cohort 4: no interventions were administered

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
DES-9384

Primary outcome(s)
Safety and tolerability of DES-9384 measured using incidence of adverse events (AEs), physical examinations, and change from baseline for vital signs, ECGs and clinical laboratory tests at Day -1 until the follow-up visit. The incidence of AEs is not measured at granular timepoints but for the other measurements they are as follows:

Part 1:
1. ECGs and vital signs are taken at Day -1, pre-dose, 1 h, 4 h, 8 h, 12 h, 13 h, 16 h, 24 h and 48 h post-morning dose, and the follow up visit (up to day 7 post-dose)
2. Clinical laboratory tests are taken at Day -1, pre-dose, 48 h post-morning dose and the follow up visit (up to day 7 post-dose)

Part 2:
1. ECGs and vital signs are taken at Day -1, pre-dose, Day 1 (1 h, 4 h, 12 h post-morning dose) and Day 7 (1 h, 4 h, 12 h post-morning dose), 24 h post-final dose, 48 h post-final dose and the follow up visit (up to day 7 post-final dose).
2. Clinical laboratory tests are taken at Day -1, Day 4 pre-morning dose, Day 7 pre-morning dose, 24 h post-final dose, and the follow up visit (up to day 7 post-final dose)

Key secondary outcome(s)
1. PK parameters: Tlag, Tmax, Cmax, C12, C24, AUC(0-12), AUC(0-24), AUC(0-last), AUC(0-tau), AUC(0-inf),T1/2, Aeu and associated renal clearance (CLr) for DES-9384, as applicable measured using plasma concentration data (Parts 1 and 2) and urine concentration data (Part 1 only) at Day -1 (Part 1) or Day 1 (Part 2) until discharge

Part 1:
Urine samples will be taken pre-dose in the 24 h period before the morning dose and then at the following intervals 0-4, 4-8, 8-12, 12-24, 24-48 h post-morning dose.
Plasma samples will be taken pre-dose, 0.5 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 12.5 h, 13 h, 14 h, 16 h, 18 h, 24 h and 48 h post-morning dose, and the follow up visit (up to day 7 post-final dose)

Part 2:
Plasma samples will be taken pre-morning dose, Day 1 (0.5h, 1h, 2h, 4h, 6h, 8h, 12h, 12.5h, 13h, 14h, 16h, 18h post-morning dose) and Day 7 (0.5h, 1h, 2h, 4h, 6h, 8h, 12h, 12.5h, 13h, 14h, 16h, 18h post-morning dose), 24h post-final dose, 48h post-final dose and the follow up visit (up to day 7 post-final dose).

2. PK parameters: Tmax, Cmax, C12, C24, AUC(0-12), AUC(0-24), AUC(0-last), AUC(0-inf), Ae, associated CLr and Frel (fed vs fasted) for DES-9384, as applicable (Part 1 only) measured using Plasma concentration data and urine concentration data at Day -1 until discharge

Part 1:
Urine samples will be taken pre-dose in the 24 h period before the morning dose and then at the following intervals 0-4, 4-8, 8-12, 12-24, 24-48 h post-morning dose.
Plasma samples will be taken pre-dose, 0.5 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 12.5 h, 13 h, 14 h, 16 h, 18 h, 24 h and 48 h post-morning dose, and the follow up visit (up to day 7 post-final dose)

Completion date
29/02/2024

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 or non-pregnant, non-lactating females of non-childbearing potential
6. Body mass index (BMI) of 18.0 to 32.0 kg/m2 as measured at screening
7. Weight 110 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
All

Total final enrolment
88

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 serious adverse reaction or serious hypersensitivity to the challenge agent (AITC) or

vehicle (mineral oil) (subjects participating in the skin challenge assessments in Part 1 Cohort 2, 4 or 7 only)
4. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease (intermittent history of vomiting or diarrhoea), neurological or psychiatric disorder, as judged by the investigator
5. Subjects with a history of cholecystectomy or gall stones
6. History of dermatographism (subjects participating in the skin challenge assessments in Part 1 Cohort 2, 4 or 7 only)
7. Presence or history of clinically significant skin disorders, as judged by the investigator (Part 1 only)
8. History of trauma or surgery (laceration repair is not excluded) to the forearm but not including wrist or hand injury/surgery (subjects participating in the skin challenge assessments in Part 1 Cohort 2, 4 or 7 only)
9. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
10. Excessive tattoos, forearm hair or other physical or behavioural characteristics which may interfere with PD objectives of the study, as determined and agreed by the PI and sponsor (subjects participating in the skin challenge assessments in Part 1 Cohort 2, 4 or 7 only) Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are not allowed.
11. The following laboratory evaluations at screening or first admission, including:
– RBC or haemoglobin < lower limit of normal (LLN)
– ALT or AST > upper limit of normal (ULN)
12. Blood pressure (supine) at screening or first admission outside the range of 90 to 140 mmHg systolic or 50 to 90 mmHg diastolic; and heart rate outside the range of 50 to 90 bpm.
13. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
14. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <80 mL/min/1.73m2 using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI; 2009) equation
15. Females of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative highly sensitive serum and urine pregnancy test at screening and first admission, respectively).
16. Lower than 100% dermal blood perfusion during application of AITC to the volar surface of both forearms, as assessed during screening (subjects participating in the skin challenge assessments in Part 1 Cohort 2, 4 or 7 only)
17. History or presence of known structural cardiac abnormalities, family history of long QT syndrome, cardiac syncope or recurrent, idiopathic syncope, or exercise-related clinically significant cardiac events. Any clinically significant abnormalities in rhythm, conduction or morphology of resting 12-lead ECG or clinically important abnormalities that may interfere with the interpretation of QT interval changes or QTcF >450 msec.
18. Subjects who have received any IMP in a clinical research study within the 90 days prior to the first dosing occasion or less than 5 elimination half-lives prior to Day 1, whichever is longer
19. Subjects who have previously been administered IMP in this study. Subjects who have taken part in Part 1 are not permitted to take part in Part 2
20. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
21. 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) in the 14 days before 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 PD activity is expected by the time of dosing with 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 72 h prior to dosing
23. History of any drug or alcohol abuse in the past 2 years
24. Regular alcohol consumption in males >21 units per week and in 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)
25. A confirmed positive alcohol breath test at screening or first admission
26. Current smokers and those who have smoked within the last 12 months
27. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or first admission
28. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
29. Confirmed positive drugs of abuse test result
30. Subjects who do not agree to eat a high-fat breakfast (Part 1 Cohort 4 only)
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
13/07/2023

Date of final enrolment
29/02/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
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Sponsor information

Organisation
D. E. Shaw Research

ROR
https://ror.org/02s04h872

Funder(s)

Funder type
Industry

Funder Name
D. E. Shaw Research

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available