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The study is to test the safety and tolerability of a drug called JNJ-39439335, also known as Mavatrep which is being developed for the treatment of pain from osteoarthritis

Submission date
31/10/2024

Recruitment status
No longer recruiting

Registration date
18/12/2024

Overall study status
Completed

Last Edited
09/09/2025

Condition category
Musculoskeletal Diseases

[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 purpose of this study is to test a drug called JNJ-39439335 also known as MAVATREP being developed for the treatment of pain. Mavatrep is a potent and selective Transient Receptor Potential Vanilloid cation channel, subfamily V, member 1 (TRPV1) receptor antagonist. The main objectives are to assess the pharmacokinetic profile and the safety and tolerability of the revised capsule formulation of Mavatrep using a placebo-controlled, multiple-dose cohort study in healthy volunteers followed by patients with Osteoarthritis of the knee.

Who can participate?
Up to 24 male and female healthy volunteers between the ages of 18 and 55 followed by 6 male and female participants between the ages of 25 and 79 with osteoarthritis of the knee

What does the study involve?
Multiple-dose administration of Mavatrep or placebo will occur for 21 consecutive days. A loading dose is planned to be administered twice daily on Day 1 and Day 2 while the participant remains at the site, followed by 19 days of once-daily administration of Mavatrep or placebo with a mixture of self-administration at home and site visits which include overnight stays for PK monitoring. The placebo and Mavatrep groups will both take the same amount of capsules.

What are the possible benefits and risks of participating?
Drawing blood could cause discomfort. The participant may experience lightheadedness or irritation. Having a cannula placed in an arm can cause soreness, bruising, blockage of veins and (rarely) infection. The participant may be asked to lie down before blood sampling to minimise feelings of lightheadedness. The swelling of a vein, or in very rare cases, a blood clot cannot be ruled out entirely. Infection is rare but could occur. The participant may experience local skin irritation from stickers on the skin for ECG, but these will recover quickly. It may be necessary to shave before the placing of ECG stickers.

Where is the study run from?
MAC Clinical Research

When is the study starting and how long is it expected to run for?
October 2024 to December 2025

Who is funding the study?
Early Phase Services Limited

Who is the main contact?
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008026

Protocol serial number
EPS-101

Study information

Scientific Title
A phase 1, randomised, double-blind, placebo-controlled study investigating the pharmacokinetics, safety and tolerability of multiple ascending doses of a revised capsule formulation of JNJ 39439335 (Mavatrep) in healthy participants and patients with knee pain from osteoarthritis

Study objectives
The primary objective of the study is to investigate the pharmacokinetic (PK) profile of a revised capsule formulation of Mavatrep following multiple ascending oral doses administered to healthy participants (Part 1) and patients with osteoarthritis (OA) of the knee (Part 2).

The secondary objective of the study is to assess the safety and tolerability of Mavatrep.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Submission date: 29/10/2024; pending approval

Study design
Randomized placebo-controlled double-blind parallel-group study

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied

Medical condition: Osteoarthritis
Medical condition in lay language: In osteoarthritis, the protective cartilage on the ends of the bones breaks down, causing pain, swelling and problems moving the joint. Bony growths develop, and area can become swollen and red
Therapeutic areas: Diseases [C] - Musculoskeletal Diseases [C05]

Interventions
For Healthy volunteers (Part 1), multiple-dose administration of Mavatrep or placebo will occur for 21 consecutive days. A loading dose is planned to be administered BID on Day 1 and Day 2, followed by 19 days of QD administration of Mavatrep or placebo. As BID dosing will be used for the loading dose, participants randomised to receive placebo will receive placebo BID on Day 1 and Day 2. The planned dose levels to be administered to the 3 cohorts are 3 mg (Cohort 1), 10 mg (Cohort 2) and 30 mg (Cohort 3) BID on Day 1 and Day 2, followed by QD administration of 3 mg (Cohort 1), 10 mg (Cohort 2) and 30 mg (Cohort 3) for 19 days.

For OA knee patients (Part 2), multiple-dose administration of Mavatrep or placebo will occur for 21 consecutive days. A loading dose is planned to be administered on Day 1 and Day 2, followed by 19 days of QD administration of Mavatrep or placebo; patients randomised to receive placebo will receive placebo BID on Day 1 and Day 2.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Mavatrep [Mavatrep] , Mavatrep [Mavatrep]

Primary outcome(s)
The primary endpoints of the study are the following Mavatrep PK parameters, calculated on Day 1, Day 14 and Day 21 where possible:
1. Cmax
2. tmax
3. AUC24
4. Minimum plasma drug concentration (Cmin)
5. Apparent clearance at steady state (CLSS/F)
6. Apparent volume of distribution at steady state (VdSS/F)
7. Mean residence time (MRT)
8. Accumulation ratio based on Cmax and AUC24
9. AUC0-∞ (Day 21 only)
10. t1/2
Pharmacokinetic blood samples will be also collected throughout a 3-week follow-up period to fully characterise the elimination phase of the PK profile and calculate t1/2.

Key secondary outcome(s))
The secondary endpoint of the study is the comparison of safety data between Mavatrep versus placebo as assessed by AE reporting, physical examinations, vital signs (heart rate and blood pressure), tympanic temperature, 12-lead ECG and clinical laboratory assessments on Day -1, Day 1 through to Day 42 (ET)

Completion date
18/12/2025

Eligibility

Key inclusion criteria
1. Participant is aged between 18 and 55 years old, inclusive (Part 1 only).
2. Participant is aged between 25 and 79 years old, inclusive (Part 2 only).
3. Participant has a body mass index (BMI) of ≤32 kg/m2 (Part 1) or ≤40 kg/m2 (Part 2).
4. Participant must answer all 10 questions to ensure their understanding of the Burn Prevention Measures correctly at Screening. If participants do not answer all 10 questions correctly the first time, they will be permitted to ask questions of the Investigator or study staff and take the quiz a second time.
5. Healthy and free from clinically significant illness or disease as determined by medical history, physical examination, clinical laboratory evaluations, vital signs, 12-lead ECG and other tests performed at Screening and/or Day -1 (Part 1 only). In case of uncertain or questionable results, tests performed during Screening and/or Day 1 may be repeated to confirm eligibility or judged to be clinically irrelevant for healthy participants.

Patients in Part 2 must also meet the following additional criteria before they can be randomised for treatment:
6. Patient has moderate to severe unilateral or bilateral knee OA pain (can include post-traumatic OA from historic injuries, at Investigator discretion); must be able to identify one knee as the target knee for pain assessments during the study as confirmed by:
6.1. Clinical diagnosis of OA of the knee based on criteria defined by the American College of Rheumatology. If a patient does not have radiographic evidence of OA of the target knee joint (either X-ray, computerised tomography [CT] or magnetic resonance imaging [MRI] scan) documented in their medical history within 48 months prior to Screening, they must have weight-bearing anterior-posterior tibiofemoral and lateral X-rays as part of the Screening process. If a patient has no prior diagnosis of OA but fulfils the criteria for the American College of Rheumatology for OA, they can be included in the study at the discretion of the Investigator and after confirmation of OA with radiographic evidence as part of Screening assessments.
6.2. Patients must be able to designate one target knee for the purpose of pain assessments during the study (the pain in the knee target joint should exceed the pain experienced in other joints [including the contralateral knee joint and/or ipsilateral hip joint] and pain experienced from any concomitant condition).
7. Baseline score of ≥4 to ≤9 on an 11-point NRS ('on a scale of 0 to 10, where 0 = no pain and 10 = worst imaginable pain, how would you rate your level of pain in the past 24 hours?') calculated as the average pain intensity during the last 7 days prior to randomisation (patients need to have a minimum of 5 out of 7 possible assessments [QD assessments, 24-hour average NRS]).
8. Medically stable based on physical examination, medical history, vital signs, 12 lead ECG and clinical laboratory tests including thyroid stimulating hormone (TSH) performed at Screening and Day -1. If there are abnormalities, they must be consistent with the underlying illness in the study population. If the results of the serum chemistry panel (including liver enzymes), haematology, or urinalysis are outside the normal reference ranges, the patient may be included only if the Investigator judges the abnormalities or deviations from normal to be not clinically significant or to be appropriate and reasonable for the population under study. This determination must be recorded in the patient's source documents and initialled by the Investigator. In case of uncertain or questionable results, tests performed during Screening and /or Day 1 may be repeated to confirm eligibility or judged to be clinically irrelevant for the population under study.

8. Patient must be willing and able to discontinue any pain medication (apart from paracetamol if needed for OA knee pain relief) from at least 7 days prior to Day -1 until the end of the study. Acetaminophen/paracetamol is allowed as rescue medication if dosed at up to 4 g/day if required for OA knee pain relief.

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
79 years

Sex
All

Key exclusion criteria
1. Have occupations or hobbies in which they are at high risk of sustaining thermal burns.
2. Previous enrolment and dosing in this or other trials with Mavatrep.
3. Received prior treatment with any other TRPV1 antagonist or agonist.
4. History of, or current evidence of prolonged QTcF interval >450 msec for male participants or >470 msec for female participants, or a QTcF interval <350 msec, at Screening or Day -1, or a family history of long or short QT syndrome or Torsades de Pointes.
5. Significant renal dysfunction, defined as creatinine clearance calculated using the Cockcroft-Gault equation <60 mL/min (Part 1) or <45 mL/min (Part 2).
6. Significant suicide risk as defined in the protocol.
7. History of malignancy within the past 5 years prior to Screening except for appropriately treated: cutaneous basal cell or squamous cell cancers; cured cervical cancer/cervical cancer in-situ; and (Part 2 only) low-grade stable prostate cancer.
8. Known allergies, hypersensitivity, or intolerance to Mavatrep or its excipients.
9. Any new or unresolved neurologic deficits, including progressive deficits, within 6 months before Screening. Transient neurologic deficits that are resolved within this period can be allowed if approved by the Investigator.
10. History of epilepsy or other seizure disorder.
11. Medical history of significant liver insufficiency; chronic hepatitis B or C, or human immunodeficiency virus (HIV), presence of active hepatitis B or C within the past 3 months.
12. Clinically relevant history of hypersensitivity, allergy, or contraindication to paracetamol /acetaminophen (or ingredients).
13. The participant received botulinum toxin or any other neurotoxin injections within 6 months prior to dosing.
14. Active peripheral neuropathy, paraesthesia or dysesthesia, or any other previously diagnosed neurologic condition causing paraesthesia and dysaesthesia.

Patients in Part 2 who meet any of the following additional criteria will be excluded from study participation:
15. Has any other chronic pain condition that, in the Investigator’s opinion, would interfere with the patient’s ability to assess their OA pain.
16. Any patient with radiographic evidence of another disease which may be contributing to their knee pain (including but not limited to osteonecrosis, severe malalignment, benign or malignant bony lesions) will be excluded.
17. Intra-articular injections into the target knee of either corticosteroid (within 3 months of dosing) or hyaluronan (within 1 month of dosing). Intra-articular injections of corticosteroid into any other joint within 1 month of dosing.
18. Use of topical capsaicin (e.g., creams, patches) within 1 week of dosing, or intra-articular use of capsaicin within 1 month of dosing.
19. History and clinical signs at the target knee joint of any other type of arthropathy (including but not limited to rheumatoid arthritis, psoriatic arthritis, septic arthritis, gout, pseudogout, metabolic and autoimmune arthropathies).
20. Severe depression as defined by a score of ≥29 on the Beck Depression Inventory®–II (BDI-II) at Screening.

Date of first enrolment
31/01/2025

Date of final enrolment
23/08/2025

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
MAC Clinical Research

Funder(s)

Funder type
Industry

Funder Name
Early Phase Services Limited

Results and Publications

Individual participant data (IPD) sharing plan
No Individual Participant Data (IPD) and other supporting materials will be made available to external researchers. That said, the datasets generated during and/or analysed during the current study are/will be available upon request from Dr S Vincent, shoonavincent@macplc.com, the clinical study report with data anonymisation will be shared with the relevant regulatory bodies and associated patient groups. In addition, the study will be published as a supplement to the original Mavatrep publications.

IPD sharing plan summary
Available on request, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version Part 2	10/12/2024	10/02/2025	No	Yes
Participant information sheet	Part 1 version 3.0	10/12/2024	10/02/2025	No	Yes