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A study in healthy volunteers to investigate the safety and tolerability of a new test medicine (MMV367)

Submission date
05/05/2022

Recruitment status
No longer recruiting

Registration date
24/06/2022

Overall study status
Completed

Last Edited
12/12/2023

Condition category
Infections and Infestations

[X] 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 Sponsor is developing the test medicine, MMV367, for the potential treatment of uncomplicated malaria in adults and children. Malaria is a life-threatening infection that is spread to people by mosquitoes. If left untreated, malaria can lead to death. According to the World Health Organization (WHO), an estimated 627,000 people died of malaria in 2020. This three-part, first-in-human, healthy volunteer study aims to assess the safety and tolerability of the test medicine as well as how it is taken up by the body when given as single and multiple doses. The effect of food on the test medicine will also be investigated.

Who can participate?
Healthy volunteers aged between 18 and 55 years

What does the study involve?
In Part 1, up to 40 volunteers will be split into up to 5 groups and will receive single oral doses of the test medicine or dummy medicine (placebo), at different dose levels. In Part 2, up to 8 volunteers will receive one oral dose of the test medicine in the fed state and one oral dose in the fasted state. In Part 3, up to 24 volunteers will be split into up to 3 groups and will receive single oral daily doses of the test medicine or placebo for 3 consecutive days. Volunteers' blood and urine will be taken throughout the study for analysis of the test medicine and for their safety. In Part 1 and Part 3, volunteers will be discharged from the clinical unit 4 days after the final dose of the test medicine and will return to the clinical unit on two occasions for safety assessments to be performed. In Part 2, volunteers will be discharged from the clinical unit 4 days after the final dose of the test medicine and will return to the clinical unit on a single occasion for safety assessments to be performed. Volunteers are expected to be involved in this study for approximately 6 weeks for all study parts, from screening to the final return visit.

What are the possible benefits and risks of participating?
There are no benefits of participating as this is a healthy volunteer study. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. In order to reflect the majority

patient population, male volunteers and non-pregnant and non-lactating female volunteers will be enrolled in this study. As standard reproductive toxicity studies have not yet been conducted, both male and female volunteers enrolled in this study will be required to follow the contraception requirements. Female volunteers must also have a negative pregnancy test at screening and admission.
There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation. Volunteers may experience side effects from the test medicine. Full information on possible side effects is provided to volunteers in the PIS/ICF. When investigating new medicines there is also a risk of unexpected side effects and occasionally allergic reactions. All volunteers will be closely monitored during the study and safety assessments will be performed at regular intervals. Risks are further mitigated by ensuring that only volunteers who meet all inclusion/exclusion criteria are included and that if the safety of any volunteer represents a concern they will be withdrawn. There will be an extended period of fasting for the volunteers taking part in this study. Subjects will be allowed water up to 1 hour before the scheduled dosing time and will be provided with 240 ml of water at 1-hour post-dose. Water will be allowed ad libitum after 1-hour post-dose. Decaffeinated fluids will be allowed ad libitum from lunchtime on the day of dosing. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.

Where is the study run from?
Medicines for Malaria Venture (Switzerland)

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

Who is funding the study?
1. Medicines for Malaria Venture (Switzerland)
2. GlaxoSmithKline (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-000918-33

Integrated Research Application System (IRAS)
1005344

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number

Study information

Scientific Title
A first-in-human, single-centre, single ascending dose, multiple-dose and pilot food effect study to assess the safety, tolerability and pharmacokinetics of MMV367 in healthy participants

Acronym
QSC207031

Study objectives
Primary objectives:
1. To assess the safety and tolerability of single and multiple oral doses of MMV367 in healthy participants

Secondary objectives:
1. To assess the pharmacokinetics (PK) of single and multiple doses of MMV367 in plasma (Parts 1, 2 and 3)
2. To assess the effect of a high-fat meal on the PK of a single dose of MMV367 in healthy participants (Part 2 only)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/06/2022, Fast Track REC (2 Redman Place, Stratford, London, E20 1JQ, UK; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0068

Study design
Double-blind randomized placebo-controlled cross over trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Plasmodium falciparum malaria

Interventions
Part 1:
Participants will be randomised to receive a single oral dose of MMV367 or placebo.

Part 2:
Participants will be randomised to receive two single oral doses of MMV367, once in the fasted state and once in the fed state, across two periods.

Part 3:
Participants will be randomised to receive once-daily doses of MMV367 or placebo for 3 days.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
MMV367

Primary outcome(s)
Incidence of adverse events (AEs), physical examinations and change from baseline for vital signs, electrocardiograms (ECGs) and laboratory safety tests, assessed throughout the trial from screening until discharge

Key secondary outcome(s))
1. PK parameters such as AUC, Tmax, Cmax, CL/F, Vz/F, T1/2 and AR, when applicable, measured from Day 1 to Day 7 in Part 1 of the study, Day 1 to Day 14 in Part 2 of the study and Day 1 to Day 9 in Part 3 of the study
2. PK parameters such as AUC, Tmax, Cmax and Frel, as appropriate, under fed and fasted conditions, measured from screening to Day 14 in Part 2 of the study

Completion date
25/01/2023

Eligibility

Key inclusion criteria
Informed consent and compliance:
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study

Demographics and contraception:
3. Aged 18 to 55 years inclusive at the time of signing the informed consent
4. Must agree to adhere to the contraception requirements

Baseline characteristics:
5. Healthy males or non-pregnant, non-lactating healthy females.
6. Body mass index (BMI) of 18.0 to 32.0 kg/m^2 as measured at screening
7. Weight ≥50 kg at screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or the 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 clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator
4. Blood pressure (supine) at screening or admission outside the range of 90 to 140 mmHg systolic or 50 to 90 mmHg diastolic; and pulse rate outside the range of 45 to 100 bpm, unless deemed not clinically significant by the investigator
5. A decrease of SBP ≥ 20 mmHg after 3 min standing and/or a decrease of DBP ≥10 mmHg after 3 min standing, at screening
6. History or presence of known structural cardiac abnormalities, family history of long QT syndrome, cardiac syncope or recurrent, idiopathic syncope, exercise-related clinically significant cardiac events. Any clinically significant abnormalities in rhythm, conduction or morphology of resting ECG or clinically important abnormalities that may interfere with the interpretation of QT interval changes
7. Presence of sinus node dysfunction, clinically significant PR interval prolongation (>210 msec), intermittent second- or third-degree atrioventricular block, complete bundle branch block, sustained cardiac arrhythmias including (but not limited to) atrial fibrillation or supraventricular tachycardia; any symptomatic arrhythmia with the exception of isolated extra systoles, abnormal T wave morphology which may impact on the QT/QTc assessment, or QTcF >450 msec. Participants with borderline abnormalities may be included if the deviations do not pose a safety risk, and if agreed between the sponsor's medical monitor and the investigator
8. Participants with a history of cholecystectomy or gall stones
9. Participants with conditions that affect their ability to smell or taste including, but not limited to mouth ulcers, gum disease, nasal surgery and smell and/or taste disorders (e.g. dysosmia, dysgeusia, respiratory and/or sinus infection or cold). Part 1 only.
10. Participants who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
11. Evidence of current SARS-CoV-2 infection
12. Clinically significant abnormal clinical chemistry, haematology, coagulation or urinalysis as judged by the investigator Participants with Gilbert's Syndrome are not allowed.
13. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
14. Females who are pregnant or lactating (all female participants must have a negative highly sensitive serum pregnancy test at screening and a negative urine pregnancy test at admission)
15. Participants who have received any IMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer
16. Participants who have previously been administered IMP in this study. Participants who have taken part in Part 1 are not permitted to take part in Parts 2 and 3 and participants who have taken part in Part 2 are not permitted to take part in Part 3

17. Donation of blood or plasma within the previous 3 months or loss of greater than 400 ml of blood
18. Participants 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, hormonal contraception or HRT) in the 14 days before first IMP administration
19. Participants who have received a COVID-19 vaccine within 7 days before the first IMP administration
20. History of any drug or alcohol abuse in the past 2 years
21. Regular alcohol consumption in males >21 units per week and 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)
22. A confirmed positive alcohol breath test at screening or admission
23. Current smokers and those who have smoked within the last 12 months
24. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
25. Confirmed positive drugs of abuse test result
26. Participant with a vegan or vegetarian diet (Part 2 only)
27. Male participants with pregnant or lactating partners
28. A score of 20 or more on the Beck Depression Inventory (BDI-II), and/or a response of 1, 2 or 3 for item 9 of this inventory
29. Participants who are, or are immediate family members of, a study site or sponsor employee
30. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
11/07/2022

Date of final enrolment
05/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
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Sponsor information

Organisation
Medicines for Malaria Venture

ROR
https://ror.org/00p9jf779

Funder(s)

Funder type
Charity

Funder Name
Medicines for Malaria Venture

Alternative Name(s)
MMV

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Switzerland

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available. The findings of this Phase I study will be shared with the Sponsor, Medicines for Malaria Venture (MMV) and the co-funder of the study, GSK, only. As these findings are confidential due to commercial sensitivity, it is not appropriate to share the results of this study with other researchers at this time.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes