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A 2-part study to investigate the safety, tolerability and effect of MB272 in healthy volunteers

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Registration date 16/06/2025	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 16/06/2025	**Condition category** Other	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

The purpose of this study was to investigate the study drug GS-0272 (formerly known as MB272). The overall objectives of the study were to determine the safety, tolerability (degree to which side effects of a drug can be tolerated) and concentration in the blood of the study drug when evaluated in different conditions i.e., different dose strengths, following administration of single doses, and following administration in two different forms (either as an intravenous infusion – an infusion directly into a vein or as a subcutaneous injection – an injection into the tissue layer between the skin and muscle). The study also aimed to evaluate the effect of the study drug on the body (known as pharmacodynamics), through the collection of blood samples at different times through the day.

Who can participate?

A total of 80 participants fully completed this study. Participants were healthy adult males and females of non-childbearing potential aged between 18 and 65.

What does the study involve?

The purpose of Part A was to evaluate the study objectives when GS-0272 was given as a single dose on one occasion at different dose strengths and by different routes of administration. Part A consisted of 10 groups of up to 8 participants per group: each investigating a different dose strength of GS-0272 starting at the lowest dose and gradually increasing in each group. 8 out of the 10 groups received GS-0272 or a placebo (which contained no active drug) in the form of an intravenous infusion on one occasion (Day 1) with two groups who received GS-0272 or a placebo in the form of a subcutaneous injection on one occasion (Day 1). Part A of the study consisted of a screening visit (between 28 and 2 days prior to first dose), 1 treatment period (consisting of 6 days with 5 overnight stays), 6 return visits (Days 8, 15, 22, 29, 43 & 57) and a post-study follow-up visit on Day 85.

Blood samples were taken at set time points throughout the study in order to measure the concentration profile of GS-0272 in the blood and to measure for other markers as described above. The results from each of the groups in Part A have been compared to determine if there

are any significant differences in the safety profile of GS-0272, the concentration of GS-0272 in the blood and how this changed over time. In addition, the results have been compared to determine whether there are any differences between different dose strengths as single doses and different routes of administration.

What are the possible benefits and risks of participating?
Taking part in this study was not expected to provide participants with any direct medical benefit. However, the information we get from this study may help improve the treatment of autoimmune diseases.

Possible risks include the following:
Blood Sampling: The procedure for blood collection either by direct venepuncture or indwelling cannula may cause mild pain and bruise at the collection site. Placement of an indwelling catheter is proposed in order to minimise these effects for rapid PK sampling. Very rarely, a blockage of a vein or a small nerve injury can occur, resulting in numbness and pain. If this occurs, it will resolve with time.

Blood pressure and pulse rate: The participant's blood pressure and pulse will be measured using an inflatable cuff which will be placed on the arm. They may experience mild discomfort in the arm whilst the cuff is inflated.

ECG: Small sticky pads will be placed on the participants' upper bodies before the ECG and an ECG machine will measure the electrical activity of the participant's heart. Before the pads are applied, the skin needs to be cleaned. Trained staff may need to shave/clip small patches of the participant's hair in these areas. Like Elastoplast® these sticky pads may be uncomfortable to remove.

Drug Administration: It is possible that administration of the drug may cause some mild discomfort, irritation and bruising at the site of the infusion/injection but this should resolve within a couple of days. We will also be monitoring for any specific reactions at the injection site and will provide appropriate treatment and care for these reactions as deemed necessary.

COVID-19 Risks: Participants should also be aware of the risks of exposure to COVID-19. When participants attend the clinical unit at each visit, they may be asked to complete a self-declaration form and temperature check to confirm that they are not showing any early signs of COVID-19 infection and that they have not had any contact with individuals who are currently self-isolating or have tested positive (dependent on risk mitigation measures employed at the clinical unit at the time of clinical conduct).

Participants may also be required to have a negative COVID-19 test prior to admission to the clinical unit for any overnight stays as defined within the study protocol. This procedure may cause some mild discomfort in the nose or throat when the swab is being taken but this should resolve after the procedure has been completed.

Additionally, at the clinical unit, participants may be asked to wear a facemask during procedures where clinical staff cannot maintain a 2 m distance. It is noted that if participants have a medical exemption from wearing a face mask, they will not be required to do so. In any circumstance, to prevent risk of transmission between staff and participants, all staff will be wearing appropriate personal protective equipment i.e., face masks, face shields etc during the course of the study.

Harm to the unborn child: The study is only intending to enrol females of non-childbearing potential and therefore, there are no perceived risks for females in this study. For males with

partners of childbearing potential, participants must not father a child during this study or for a safety period of 3-months following the last dose of GS-0272. Healthy volunteers must agree to use one highly effective or two effective forms of contraception with a condom (if applicable) during the study and for at least 3 months following the last dose of GS-0272.

Throughout the study the health of the participants will be regularly monitored and appropriate treatment for any medical condition will be provided if required. All doctors employed by Simbec-Orion are trained and certified in Advanced Life Support Procedures in order to deal with a medical emergency. Nurses and other clinical staff are also trained in emergency procedures. Simbec-Orion also has an agreement with Prince Charles Hospital for referral of participants if required following a medical emergency.

Where is the study run from?
The study will be conducted at Simbec-Orion Clinical Pharmacology Unit, an MHRA Phase 1 accredited CRO based in South Wales.

When is the study starting and how long is it expected to run for?
May 2022 to May 2024.

Who is funding the study?
This study is funded and sponsored by Gilead Science, Inc., based and headquartered in the United States of America (USA).

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
2021-006193-23

Integrated Research Application System (IRAS)
1005463

ClinicalTrials.gov (NCT)
Nil Known

Protocol serial number
MB272-001

Study information

Scientific Title
A two-part phase 1, first in human study to evaluate the safety and tolerability of single and multiple ascending intravenous and subcutaneous doses of a monoclonal antibody (MB272) in healthy adults

Study objectives
The primary objective of this study is:
1. To determine the safety and tolerability of different dose levels of a single dose (Part A) or multiple doses (Part B, if conducted) of GS-0272 in healthy participants

The secondary objectives of this study are:
1. To evaluate the pharmacokinetics (PK) of GS-0272 in healthy participants
2. To determine the extent and duration of receptor engagement after single and repeat (if conducted) administrations of GS-0272 in healthy participants (as applicable)
3. To determine the incidence of antidrug antibodies (ADA) after single and repeat (if conducted) administrations of GS-0272 in healthy participants (as applicable)

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 12/05/2022, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2922 941119; Wales.REC2@wales.nhs.uk), ref: 22.WA.0123

2. approved 16/06/2022, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, United Kingdom; +44 (0) 20 3080 6000; info@mhra.gov.uk), ref: CTA 55486/0001/001-0001

Study design

A two-part first-in-human interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Other, Safety

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
This was a Phase 1, first-in-human, randomised, double-blind study to evaluate the safety, tolerability, PK, pharmacodynamics (PD) and immunogenicity of different dose levels of GS-0272, a monoclonal antibody targeting immune cell receptors expressed on B- and T-cells, in healthy participants.

The study was planned to be conducted in 2 parts (Part A and B); however, Part B was considered optional and following discussions with the study Sponsor, it was determined that the conduct of Part B was not required. The study enrolled 80 participants in Part A and each participant was assigned to one cohort in Part A.
Part A followed a single ascending dose design and included 80 healthy participants in 10 cohorts of up to 8 participants each (Cohorts A1 to A10). Participants were randomised 3:1 to receive one dose of GS-0272 (6 participants) or placebo (2 participants) per cohort. Eight of the SAD cohorts received GS-0272 (or placebo) administered via IV route and two SAD cohorts received GS-0272 (or placebo) administered via SC injection.

Part A (SAD) healthy participants undertook a screening period (Day -28 to Day -2), an in-house treatment period comprising of 6 days / 5 overnight stays (Day -1 to Day 5) and then subsequent ambulatory visits on Days 8 (Week 2), 15 (Week 3), 22 (Week 4), 29 (Week 5), 43 (Week 7), 57 (Week 9) for study assessments and end of study visit procedures which were performed at the final visit Day 85 (Week 13).

Part A was conducted at the Simbec-Orion Clinical Pharmacology (Clinical Unit) under full medical and nursing supervision.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
GS-0272 100 mg/mL solution for intravenous infusion or subcutaneous injection (formerly known as GS-0272)

Primary outcome(s)
1. Adverse Events are recorded from the point of informed consent up to final post-study follow up visit in each part
2. Laboratory safety (biochemistry, haematology, coagulation and urinalysis) is measured at set timepoints from screening through to post-study follow up visit (Day 85)

3. Vital signs (systolic/diastolic blood pressure, heart rate, oral body temperature) are measured at set timepoints from screening through to post-study follow up visit (Day 85)
4. 12 lead ECG (heart rate, RR interval, PR interval, QRS duration, QT interval, QTcF interval) is measured at set timepoints from screening through to post-study follow up visit (Day 85)
5. Infusion/Injection Site Reaction is measured at set timepoints from screening through to post-study follow up visit (Day 85)

Key secondary outcome(s))
Measured using plasma concentration analysis at set timepoints from screening through to post-study follow up visit (Day 85):
1. Cmax
2. Tmax
3. λz
4. t1/2
5. AUC0-tlast
6. AUC0-inf
7. AUC%extrapolated
8. Total body clearance (CL)
9. Vz
10. CL/F (SC administration only)
11. Vz/F (SC administration only)

Completion date
28/05/2024

Eligibility

Key inclusion criteria
1. Healthy males and female participants, between ≥18 and ≤65 years of age, inclusive.
2. Female participant of non-childbearing potential. For the purposes of this study, this is defined as the participant being amenorrhoeic for at least 12 consecutive months or at least 4 months post-surgical sterilisation (including bilateral oophorectomy with or without hysterectomy).
3. Female participant with a negative pregnancy test at screening.
4. Female participant of menopausal status as defined by no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level falls within the respective postmenopausal pathology reference range may be used to confirm a postmenopausal state in females not using hormonal contraception or hormonal replacement therapy. A single FSH measurement is insufficient in the absence of 12 months of amenorrhea.
5. Participants assigned male at birth (and partner of childbearing potential) willing to use a highly effective method of contraception or 2 effective methods of contraception, if applicable (unless anatomically sterile or where abstaining from heterosexual intercourse is in line with the preferred and usual lifestyle of the participant) from first dose until 3 months after last dose of IMP.
6. Participant with a body mass index (BMI) of 18-30 kg/m^2. BMI = body weight (kg) /[height (m)]^2.
7. No clinically significant history of previous allergy / sensitivity to GS-0272 or any of the excipients contained within the IMP.
8. No clinically significant abnormal test results for serum biochemistry, haematology and/or urine analyses within 28 days before the first dose administration of the IMP.
9. Participant with a negative urinary drugs of abuse (DOA) screen (including alcohol) test results, determined within 28 days before the first dose administration of the IMP (N.B.: A

positive test result may be repeated at the Investigator’s discretion).
10. Participant with negative human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg) and hepatitis C virus antibody (HCV Ab) test results at screening.
11. No clinically significant abnormalities in 12-Lead electrocardiogram (ECG) (e.g. a PR interval ≤ 220 ms, QRS width ≤ 120 ms, QT interval corrected using Fredericia’s formula QTcF ≤ 450 ms) determined within 28 days before first dose of IMP.
12. No clinically significant abnormalities in vital signs (e.g., blood pressure, systolic blood pressure ≤ 140 mmHg, diastolic blood pressure ≤ 90 mmHg, heart rate ≥ 40 or ≤ 100 bpm, oral temperature) determined within 28 days before first dose of IMP.
13. Participant must be available to complete the study (including all follow-up visits).
14. Participant must satisfy an Investigator about his/her fitness to participate in the study.
15. Participant must provide written informed consent to participate in the study.
16. Participants with a negative COVID-19 test on admission (if required).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment
80

Key exclusion criteria
1. Presence of any significant acute or chronic, uncontrolled medical/ psychiatric illness.
2. History or evidence of clinically relevant immunological disorders, or other autoimmune disease, or known immunodeficiency of any cause (e.g., rheumatoid arthritis, lupus erythematosus, scleroderma, etc).
3. Use of prescription or non-prescription drugs, including vitamins, herbal and dietary supplements within 28 days or 5 half-lives (whichever is longer) prior to the first dose of IMP.
4. Evidence of renal, hepatic, central nervous system, respiratory, cardiovascular or metabolic dysfunction.
5. A clinically significant history of drug or alcohol abuse (defined as the consumption of more than 14 units [for male and female participants] of alcohol a week) within the past two years.
6. Inability to communicate well with the Investigators (i.e., language problem, poor mental development or impaired cerebral function).
7. Participation in a New Molecular Entity (NME) clinical study within the previous 3 months or five half-lives, whichever is longer, or a marketed drug clinical study within the 30 days or five half-lives, whichever is longer, before the first dose of IMP. (Washout

period between studies is defined as the period of time elapsed between the last dose of the previous study and the first dose of the next study).
8. Receipt of immunoglobulin or other blood products within 3 months prior to screening.
9. Receipt of a vaccine within 60 days prior to screening.
10. Receipt of any systemic immunosuppressant agent, antibody or biologic medicinal product within 6 months prior to screening.
11. Receipt of any systemic steroid within 2 months prior to screening.
12. Donation of 450 mL or more blood within the 3 months before the first dose of IMP.
13. History of allergic disease or reactions likely to be exacerbated by any component of GS-0272.
14. Malignancy within 5 years prior to screening with the exception of specific cancers that are cured by surgical resection (e.g. except basal cell skin carcinoma of the skin and cervical carcinoma). Participants under evaluation for possible malignancy are not eligible.
15. Significant cardiac disease or unstable uncontrolled cardiac disease.
16. Any other finding that, in the opinion of the Investigator, deems the participant unsuitable for the study.
17. Vegans, vegetarians or other dietary restrictions (e.g., restrictions for medical, religious or cultural reasons, etc).
18. Users of nicotine products i.e., current smokers or users of cigarette replacements (i.e., ecigarettes, nicotine patches or gums) with consistent use of > 5 cigarettes/replacements per day.
19. Female participants who are pregnant, breastfeeding or lactating.

Date of first enrolment
07/07/2022

Date of final enrolment
05/03/2024

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Simbec House Merthyr Tydfil Industrial Park
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Sponsor information

Organisation
Gilead Sciences (United States)

ROR
https://ror.org/056546b03

Funder(s)

Funder type
Industry

Funder Name
Gilead Sciences

Alternative Name(s)
Gilead, Gilead Sciences, Inc., Oligogen

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes