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A phase II Study of obexelimab in patients with relapsing multiple sclerosis

Submission date
11/06/2024

Recruitment status
No longer recruiting

Registration date
26/11/2024

Overall study status
Completed

Last Edited
16/01/2025

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Multiple sclerosis (MS) is a potentially disabling autoimmune disease that affects the central nervous system (brain and spinal cord). B cells play an important role in the autoimmune disease mechanism. Obexelimab, an experimental study drug, is an antibody developed for the treatment of such autoimmune disorders. The drug acts by binding to the B cell surface and decreases B cell activity. The purpose of this study is to evaluate the safety and effectiveness of obexelimab, on MS.

Who can participate?
Patients ≥ 18 to ≤ 60 years of age with a diagnosis of relapsing-remitting or secondary progressive with relapses (RMS)

What does the study involve?
In Part A, obexelimab or placebo as subcutaneous injections, will be administered at random. Two-thirds of the patients will receive obexelimab and one-third will receive a placebo, once weekly for 12 weeks. After week 12, all patients will receive obexelimab in Part B, for an additional 12 weeks.

What are the possible benefits and risks of participating?
Taking part in this study may or may not help to treat the patient's MS, however, the data collected may help doctors learn more about the study drug and whether it provides any benefit to patients with MS, which in turn may help future patients with MS.

All drugs have some risks, which may include things that could make the participant feel unwell, uncomfortable, or harm them.
Participants might have side effects related to the study drug and procedures while taking part in the study. Everyone taking part in the study will be watched for side effects; however, the study team do not know all the side effects that the study drug may have on the participant. These effects may be mild or serious. In some cases, these effects might be long-lasting, permanent, and may even be life-threatening. Participants should call the study doctor when they think they are having any problems.
The sponsor recognises that weekly IP administration is quite intensive, therefore the burden of

this has been mitigated for visits where no clinic attendance is required by protocol, by allowing the option of home IP administration either via self, caregiver or utilisation of home care vendor services (Firma). IP administration is the only study procedure that Firma would be undertaking if required.

Obexelimab risks:
There have been 198 healthy volunteers and patients with autoimmune diseases treated with various doses of obexelimab as either intravenous infusion (158 patients) or subcutaneous injection (40 patients). Approximately 40 additional patients have been dosed with either obexelimab or placebo in patients with IgG4-RD and warm autoimmune hemolytic anaemia. Obexelimab affects the immune system and may cause serious infections. Obexelimab has side effects at the site of drug injection with the most common being bruising and redness. Most of these side effects were mild and lasted less than a day.
When obexelimab was given by intravenous infusion, there were serious cases of infusion reactions and non-serious abdominal discomfort including nausea, vomiting, and diarrhoea. These side effects have not been observed for obexelimab given as a subcutaneous injection.
Other common side effects included:
• Headache 8%
• Injection site bruising 8%
• Dizziness 5%
• Back pain 5%
• Injection site redness 5%
These events were mostly mild and temporary.

Risks from study test procedures:
• Injection site reactions: pain, redness, swelling, itching, or bruising at the site of the study drug injection.
• Blood sampling: Having blood taken from a vein may cause some pain, redness, or bruising at the injection site. An infection at the injection site is possible but rare.
• ECG: The ECG procedure may cause some mild discomfort during the placement and removal of the leads to and from the skin. The skin may become a little red or irritated. May also experience local irritation, redness, or burning in the areas where the leads are attached.
• MRI scan: There are risks from an MRI if participants are pregnant or have one of the following: an artificial heart valve, pacemaker, metal plate, pins, or other metallic objects in their body (including gunshot or shrapnel). Participants may also become anxious from lying in a tight space without moving. The MRI scan does not cause any pain and does not expose participants to X-ray radiation. For some MRI scans, participants may receive a contrast dye, given via vein using a small needle or plastic tube. Participants may feel local warmth or pain in the area where the dye is injected. The most common contrast material used for MRIs is gadolinium. Side effects from the dye may include nausea, vomiting, or headache. Participants will not be given the MRI contrast dye if they have abnormal kidney function. People with severe kidney insufficiency or chronic liver disease experiencing kidney insufficiency may develop a severe disease, called nephrogenic systemic fibrosis, from gadolinium. Nephrogenic systemic fibrosis triggers thickening of the skin, organs, and other tissues. The exact cause is unclear, and there is no effective treatment. Serious allergic reactions that may be life-threatening are very rare. Participants will be asked questions and may undergo tests to ensure that the MRI scan is safe for them.
• Chest X-ray: Chest X-rays involve exposure to a very small amount of ionising radiation. Ionising radiation can cause cancer many years or decades after the exposure. Participants are advised of the inherent risks in the ICF.
• Lumbar Puncture: Use of atraumatic or non-cutting lumbar puncture needles and screening techniques (ultrasound) may be used to reduce the risk of a post-lumbar puncture headache.

• Unforeseeable risks: Since obexelimab is an experimental study drug, there may be other risks that are unknown at this time. Participants are advised to seek medical assistance right away.
• Reproductive risks; The effects of obexelimab on human eggs, unborn children (including miscarriage), or nursing infants are not known at this time. Participants will not be eligible for participation if they are planning on becoming pregnant if they are pregnant, or if they are nursing.

Where is the study run from?
Zenas BioPharma (USA) LLC

When is the study starting and how long is it expected to run for?
June 2024 to January 2026

Who is funding the study?
Zenas BioPharma (USA) LLC

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06564311

Clinical Trials Information System (CTIS)
2024-512707-40

Integrated Research Application System (IRAS)
1010092

Central Portfolio Management System (CPMS)
61107

Protocol serial number
ZB012-02-002

Study information

Scientific Title
A phase II, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of obexelimab, in patients with relapsing multiple sclerosis

Study objectives
To evaluate the effect of weekly SC administration of obexelimab versus placebo in patients with RMS on the prevention of new gad enhancing T1 (GdE T1) hyperintense lesions detected using MRI

To evaluate the effect of weekly SC administration of obexelimab versus placebo in patients with RMS on:
• Additional MRI endpoints
• Neurofilament light chain (NfL)

To evaluate the safety and tolerability of weekly SC administration of obexelimab in patients with RMS

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 09/09/2024, London – Riverside REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; riverside.rec@hra.nhs.uk), ref: 24/LO/0508

Primary study design
Interventional

Study design
Randomized placebo-controlled double-blind study

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Relapsing multiple sclerosis

Interventions
Patients will be randomized 2:1 to obexelimab 250mg SC or matching placebo SC once weekly for 12 weeks, followed by an additional 12 weeks in which all patients will receive obexelimab 250mg SC. A follow-up visit will occur 8 weeks after the final dose. Randomization will be performed using Interactive Response Technology.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
Obexelimab [Obexelimab]

Primary outcome(s)
Cumulative number of new GdE T1 hyperintense lesions measured by brain MRI over Week 8 and 12

Key secondary outcome(s)
1. Cumulative number of new and/or enlarging T2 weighted hyperintense lesions measured by brain MRI over Week 8 and Week 12
2. Number of new GdE T1 hyperintense lesions measured by brain MRI at Weeks 4, 8, and 12
3. Change from baseline in volume of T2 lesions measured by brain MRI at Week 12
4. Serum neurofilament lightchain measured by a blood test at Week 12
5. Incidence of AEs, SAEs, including injection site reactions and hypersensitivity reactions, and AESI, as defined by the CTCAE v5.0 from date of informed consent until end of study

Completion date
31/01/2026

Eligibility

Key inclusion criteria
1. Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the ICF
2. Male or female, ≥ 18 to ≤ 60 years of age, inclusive, at the time of signing the ICF
3. Diagnosis of RMS (relapsing-remitting or secondary progressive with relapses) according to the 2017 revision of the McDonald diagnostic criteria
4. An EDSS of ≤ 5.5 at the Screening Visit
5. Must have documentation of:
5.1. at least 1 relapse within the previous year
OR
5.2. ≥ 2 relapses within the past 2 years
OR
5.3. ≥ 1 active Gd-enhancing brain lesion on an MRI scan within the past 6 months before screening

6. A female patient is eligible to participate if she is not pregnant, not breastfeeding, and at least 1 of the following conditions applies:
6.1. Not a woman of childbearing potential (WOCBP) as defined in Appendix 4
OR
6.2. A WOCBP who agrees to follow the contraceptive guidance in Appendix 4 until at least 8 weeks after the last administration of IMP
AND
6.3. Has a negative serum pregnancy test at screening and a negative urine pregnancy test on Day 1 before the first dose of IMP
AND
6.4. Agrees to refrain from egg donation until at least 8 weeks after the last administration of IMP
7. A male patient must:
7.1. Agree to either (i) abstain from intercourse or (ii) use contraception (as detailed in Appendix 4) until at least 8 weeks after the last administration of IMP, or (iii) be surgically sterile for the duration of the study
AND
7.2. Agree to refrain from donating sperm until at least 8 weeks after the last administration of IMP

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Key exclusion criteria
1. Primary progressive MS or secondary progressive MS without relapses
2. Meet criteria for neuromyelitis optica spectrum disorder
3. Relapse in the 30 days prior to randomization
4. ≥ 10 years disease duration from the onset with patient's EDSS ≤ 2.0 (patient-reported is adequate in absence of written medical record)
5. Has > 20 Gd+ lesions on brain MRI at screening
6. Prior use of B cell–depleting agents
7. Prior use of other biologic immunomodulatory agents ≤ 6 months before randomization
8. Has received systemic corticosteroids or adrenocorticotropic hormone within 1 month (30 days) before screening MRI
9. Has received dimethyl fumarate within 1 month before randomization
10. Has received treatment with B-interferons or glatiramer acetate within 1 month before

randomization
11. Has received treatment with intravenous immunoglobulins, plasmaphereses, sphingosine-1-phosphate treatments, or natalizumab (patients who stop getting infusions within 6 months before randomization should be ruled out for progressive multifocal leukoencephalopathy) within 2 months before randomization
12. Has received azathioprine or methotrexate within 6 months before randomization
13. Has received treatment with teriflunomide within 3 months to randomization (unless elimination procedure was done)
14. Has received cladribine, cyclophosphamide, alemtuzumab, or mitoxantrone within 2 years before randomization
15. Has received lymphoid irradiation or stem cell transplantation
16. Has received an investigational treatment or direct medical intervention on another clinical study within 12 weeks or < 5 half-lives of the investigational treatment, whichever is longer, before randomization
17. Has received a live vaccine or live therapeutic infectious agent within the 4 weeks before randomization
18. History of drug or alcohol abuse in the previous 12 months before screening in the opinion of the investigator
19. Acute hepatitis B infection (hepatitis B surface antigen-positive), active hepatitis C virus, or HIV infection. Patients will be excluded from the study if they have a positive test for active hepatitis B by detecting (a) hepatitis B surface antigen or (b) hepatitis B core antibody. In Japan, patients will be excluded if there is detection of (a) hepatitis B surface antigen, (b) hepatitis B surface antibody, or (c) hepatitis B core antibody. Patients with active, chronic or uncured HBV will be excluded.
20. Evidence of active tuberculosis (TB) or at high risk for TB as shown by at least one of the following:
20.1. Documented history of active TB or latent TB, unless completion of treatment according to local guidelines
20.2. Positive, indeterminate, or invalid interferon-gamma release assay results at screening, unless treatment is documented. Patients with an indeterminate test result can repeat the test once either centrally or locally, but if the repeat test is also indeterminate, the patient is excluded
20.3. Signs or symptoms that could represent active TB
20.4. Chest radiograph, computed tomography, or MRI that suggests possible diagnosis of TB
21. Malignancy within 5 years except successfully treated in situ cervical cancer, resected squamous cell or basal cell carcinoma of the skin
22. Hematology or clinical chemistry parameters that meet any of the following criteria at screening:
22.1. White blood cell count < 3.5 × 10^3/μL
22.2. Absolute neutrophil count < 1.5 × 10^3/μL
22.3. Elevated serum creatinine > 2.5 × upper limit of normal (ULN) OR estimated creatinine clearance < 40 mL/min calculated by the Cockcroft-Gault formula at screening
22.4. Hemoglobin < 10 g/dL
22.4. Platelet count < 75 × 10^3/μL
23. Abnormal liver function tests meeting any of the following criteria:
23.1. Alanine aminotransferase > 2 × ULN
23.2. Aspartate aminotransferase > 2 × ULN
23.3. Total bilirubin > 1.5 × ULN
24. History or evidence of a clinically unstable/uncontrolled disorder, condition, or disease (including, but not limited to, cardiopulmonary, oncologic, renal, hepatic, metabolic, hematologic, psychiatric, active infection) other than RMS that, in the opinion of the investigator, would pose a risk to patient safety or interfere with the study evaluation,

procedures, or completion
25. Any known allergy to mAb therapy
26. Hypersensitivity to dextran or components of dextran or any component of the study drug and placebo, including excipients
27. Inability to comply with MRI scanning or MRI contrast administration

Date of first enrolment
06/08/2024

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
United Kingdom

England

Wales

Austria

Belgium

China

Croatia

Denmark

Greece

Italy

Poland

Spain

United States of America

Study participating centre
The Royal London Hospital
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Study participating centre
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Study participating centre
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Study participating centre
Colchester General Hospital
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Sponsor information

Organisation
Zenas BioPharma (USA) LLC

Funder(s)

Funder type
Industry

Funder Name
Zenas Biopharma

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date. The sponsor, PPD, part of Thermo Fisher Scientific and regulatory authorities will be granted direct access to medical records for verification of study procedures and data without

violating the confidentiality of the records to the extent permitted by the applicable laws and regulations. Before data transfer all identifiable information will be replaced by a code. The sponsor shall ensure that the necessary measures are taken to protect and maintain the confidentiality of data when transferred outside of the UK and EEA.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.0	22/03/2024	29/10/2024	No	No