ISRCTN17105865 https://doi.org/10.1186/ISRCTN17105865

A study to find out the best length of time between ocrelizumab doses for patients with relapsing remitting multiple sclerosis using a trial design with multiple groups and multiple stages

Submission date 25/02/2026	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 26/03/2026	**Overall study status** Ongoing	
Last Edited 27/05/2026	**Condition category** Nervous System Diseases	

Plain English summary of protocol
Not provided at time of registration.

Contact information

Type(s)
Public

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None - REFINE-MS Team

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Additional identifiers

Integrated Research Application System (IRAS)
1013232

Sponsor's protocol code number
ND004

Study information

Scientific Title
REFINE-MS: A randomised, rater-blind, phase 3 trial to determine the optimal dose frequency of ocrelizumab for patients with relapsing remitting multiple sclerosis using a novel multi-arm multi-stage frequency-optimisation design

Acronym
REFINE-MS

Study objectives
To test whether people with relapsing-remitting MS who have been stable on ocrelizumab for a minimum of 2 years can take it less often and still keep their MS under similar control (measured by looking at whether or not there are any new signs of damage on a brain MRI scan) compared with the standard schedule of every 6 months.

Secondary objectives of REFINE-MS are: to determine the effects of taking ocrelizumab less often on how well-controlled the participant’s condition is (including whether or not their disability progresses), participant quality of life, patient reported outcomes and cost-savings to the NHS.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/04/2026, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 0207 104 8118; leicestercentral.rec@hra.nhs.uk), ref: 26/EM/0057

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Active

Assignment
Parallel

Purpose
Treatment, Safety

Study type(s)
Efficacy, Safety, Treatment, Other

Health condition(s) or problem(s) studied
Medical condition: Relapsing-remitting multiple sclerosis (RRMS)
Medical condition in lay language: A long-term condition affecting the brain and spinal cord, where people experience episodes of new or worsening symptoms (relapses) followed by periods of recovery (remission).
Therapeutic areas: Diseases [C] - Nervous System Diseases [C10]

Interventions
Participants will be randomised in the REFINE-MS electronic data capture (eDC) system to receive ocrelizumab (ocrelizumab 600mg intravenous or 920mg subcutaneous). The dose frequency depends on the arm to which the participant is randomised. This trial includes 2 Stages (Stage 1 (divided into 1a and 1b) and Stage 2. In Stage 1a, 6-monthly vs 12-monthly frequencies will be tested, with 100 patients randomised across these two arms. Following this, the study will proceed directly to Stage 1b, in which 3 additional arms will open (9-monthly, 15-monthly and 18-monthly), meaning that participants can be randomised to all five arms. An interim analysis of 12 months of data in 90 of the original 100 participants randomised to 6 vs 12 months will be carried out to determine the design of Stage 2 of the trial. If 12-monthly is not inferior to 6-monthly in terms of proportion of patients with new T2 lesions after one year, patients will continue to be recruited to all five arms; if it is inferior, the trial will convert into a 2-arm non-inferiority trial of 9-monthly vs. 6-monthly frequencies. All participants will be followed up with for at least 2 years.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ocrevus 300 mg concentrate for solution for infusion [Ocrelizumab] , Ocrevus 920 mg solution for injection [Ocrelizumab]

Primary outcome(s)
1. The proportion of participants without new T2 lesions measured using brain MRI scans at baseline, 1 year for the Stage 1 (interim) analysis and at 2 years for the Stage 2 (final) analysis

Key secondary outcome(s)
1. Number of new T2 lesions measured using brain MRI at 2 years

2. Time-to-relapse measured using the MS relapse notable events reported by site clinician at 2 years

3. Annualised relapse rate measured using the MS relapse notable events reported by site clinician at 2 years

4. Proportion of participants without disability progression (defined by Expanded Disability Status Scale (EDSS) score increase of ≥1 point or ≥0.5 point if baseline EDSS >5.5) measured using data collected by a blinded rater at site at 2 years

5. Rate of adverse events (graded by severity) and infections measured using data reported by site clinician at 2 years

6. Rate of whole brain atrophy measured using brain MRI at 2 years

7. Proportion of participants with hypogammaglobulinaemia measured using immunoglobulin laboratory test results at 2 years

8. Changes in serum neurofilament light concentration measured using laboratory tests results at 2 years

9. Changes in cognitive functions assessed by Symbol Digit Modalities Test (SDMT)) measured using data collected by a blinded rater at site at 2 years

10. Changes in quality-of-life, patient-reported outcomes, and therapy administration satisfaction measured using EuroQol EQ5D-5L, Multiple Sclerosis Impact Scale (MSIS-29) and the Client Services Receipt Inventory and Work Productivity and Activity Impairment participant-reported outcome measures (PROMs) questionnaires at 2 years

Completion date
30/09/2030

Eligibility

Key inclusion criteria
1. Adult participants aged ≥18 yrs
2. Diagnosis of RRMS, according to the 2017 or 2024 revised McDonald criteria
3. Received 4 or more 6-monthly cycles of ocrelizumab (IV or SC) according to NICE TA533 guidelines and the ocrelizumab summary of product characteristics (SPC), prior to randomisation
4. Expanded Disability Status Scale (EDSS) score between 0 and ≤6.5 inclusive at baseline
5. Participants who wish to remain on ocrelizumab
6. Written informed consent provided
7. At randomisation, participants must have a QC-approved Baseline MRI scan (per the MRI Guide), performed up to 6 weeks after the Screening/Baseline/M0 visit

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Clinical relapse(s) within 12 months prior to randomisation
2. New MRI lesions prior to randomisation, assessed by the treating site through comparison of the trial baseline scan with the most recent preceding MRI performed at least 3 months earlier while the participant was receiving ocrelizumab
3. Co-treatment with other immunosuppressive medications
4. Any condition or circumstance that prevents the participant from undergoing regular MRI scanning
5. Pregnancy or intention to become pregnant during the study period

Date of first enrolment
26/05/2026

Date of final enrolment
30/06/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
UCLH National Hospital for Neurology and Neurosurgery
Queen Square
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Study participating centre

University Hospital Coventry and Warwickshire
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Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request (following the publication of the primary outcome) from the REFINE-MS Trial Management Group (contactable via the REFINE-MS trial mailbox mrcctu.refinems@ucl.ac.uk). Data will be shared according to the Clinical Trials Unit's controlled access approach, based on the following principles:

• No data should be released that would compromise an ongoing trial or study.
• There must be a strong scientific or other legitimate rationale for the data to be used for the requested purpose.
• Investigators who have invested time and effort into developing a trial or study should have a period of exclusivity in which to pursue their aims with the data, before key trial data are made available to other researchers.
• The resources required to process requests should not be under-estimated, particularly successful requests which lead to preparing data for release. Therefore, adequate resources must be available in order to comply in a timely manner or at all, and the scientific aims of the study must justify the use of such resources.
• Data exchange complies with Information Governance and Data Security Policies in all of the relevant countries.
• Only tabulated, pseudonymised data will be shared.
• Data Transfer Agreements and relevant approvals will be sought.
• Participant consent will be sought for use of data for future research via the main trial consent form when participants join the study.

Data will be available for sharing following publication of the primary outcome. Researchers wishing to access REFINE- MS data should contact the Trial Management Group in the first instance.
Any remaining samples collected as part of the mechanistic immunology substudy will be destroyed at the end of the trial and therefore will not be available for future research.

IPD sharing plan summary

Available on request