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Masitinib in patients with primary progressive or secondary progressive multiple sclerosis

Submission date
05/04/2022

Recruitment status
No longer recruiting

Registration date
20/05/2022

Overall study status
Completed

Last Edited
07/06/2022

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] 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 an inflammatory neurodegenerative disease of the central nervous system (CNS). The vast majority of MS drugs primarily benefit active/relapsing forms of MS with limited efficacy in the progressive forms. It is estimated that 10-15,000 people have primary progressive MS in the UK.
Masitinib is a new chemical entity under development in progressive forms of multiple sclerosis. Masitinib targets newly discovered disease mechanisms via its dual action against activated macrophage/microglia and mast cells.

Who can participate?
Patients with primary and secondary progressive MS without relapse will be eligible to be treated during the study.

What does the study involve?
Patients will be treated for 96 weeks with masitinib or placebo. They will be then offered the option to participate in open-label extension. As part of the study, patients will have a physical exam, vital signs, and neurological exam. They will have efficacy assessments and questionnaires to evaluate their medical condition and its progress. Patients will have ECGs to monitor cardiac safety and also routine blood samples and PK blood samples. There will be urinalysis and urine cytology. For some patients there will be regular permanency testing.

What are the possible benefits and risks of participating?
Benefits:
Participants will be reimbursed for their travel expenses upon presentation of costs' proofs.
Risks:
Masitinib is an experimental drug and there could be adverse events that are not known yet. This is why participants will be monitored closely throughout the study. Participants will need to attend regular clinic visits which could be a burden but this is the only option to monitor their safety and well-being.

Where is the study run from?
Dokumeds (Latvia)

When is the study starting and how long is it expected to run for?
March 2022 to June 2026

Who is funding the study?
AB Science (France)

Who is the main contact?
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Contact information

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Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000639-30

Integrated Research Application System (IRAS)
1005160

Central Portfolio Management System (CPMS)

52039

Protocol serial number
AB20009

Study information

Scientific Title
A 96-week, prospective, multicenter, randomised, double-blind, placebo controlled, phase 3 study to compare efficacy and safety of masitinib dose titration to 4.5 mg/kg/day versus placebo in the treatment of patients with primary progressive or secondary progressive multiple sclerosis without relapse.

Study objectives
To evaluate the efficacy and safety of oral masitinib versus placebo in the treatment of patients with primary progressive or secondary progressive multiple sclerosis without relapse.

The secondary objectives of the study are to evaluate the efficacy of masitinib compared with placebo on a range of clinical parameters of multiple sclerosis. The secondary objectives also include the assessment of safety and tolerability of masitinib as compared to placebo in terms of adverse events, vital signs, physical examination, ECG, and clinical laboratory tests.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, ref: 22/WM/0092

Primary study design
Interventional

Study design
Interventional double blind randomized parallel group placebo controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple sclerosis

Interventions
There are 2 parallel arms: mansitinib and placebo. Patients will be treated for 96 weeks and will be offered an additional treatment extension to week 108 if they have benefit. The drug is administrated orally twice a day. Drug formulation is AB1010/Masitinib (100 mg and 200 mg tablets) or placebo tablets (100 mg and 200 mg tablets). Dose: 3.0 mg/kg/day from Week 0 to Week 4, and then to 4.5 mg/kg/day from Week 5 to Week 96/Early Temination or to Week 108. The study uses IWRS and investigators will receive notification of the arm the patient is randomized on.

Intervention Type

Drug

Phase
Phase III

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

Primary outcome(s)
Time to confirmed (12-weeks CDP [Confirmed Disability Progression]) Expanded Disability Status Scale (EDSS) progression. The EDSS progression is defined as 1-point worsening when EDSS baseline score ≤5.5 or 0.5 if baseline score >5.5 from randomization to Week 96.

Key secondary outcome(s)
1. Expanded Disability Status Scale (EDSS):
1.1. Time to confirmed (24-weeks CDP) EDSS progression. Progression is defined as 1-point worsening when EDSS score ≤5.5, or 0.5 if baseline score >5.5)
1.2. Expanded Disability Status Scale (EDSS): Absolute and ordinal change from baseline considering all measurements up to Week 96
2. Time to EDSS score of 7.0 Clinical Global Assessment Tools:
2.1. Timed 25-foot walk (T25-FW) from baseline up to Week 96 and 12 weeks confirmed worsening using 20% threshold
2.2. Nine-hole peg test (9-HPT), right and left hands sides (finger dexterity) from baseline up to Week 96 and 12 weeks confirmed worsening using 20% threshold
2.3. The Symbol Digit Modalities Test (SDMT) from baseline up to Week 96 and 12 weeks confirmed worsening using 4-point threshold
3. Brain MRI Assessments:
3.1. Brain Volume and Lesions will be measured and assessed at Baseline, Week 48 and Week 96, or early termination (only if patient discontinues after Week 48 and more than 24 weeks have elapsed since last MRI) for the following endpoints: Brain atrophy - Percent brain volume change (PBVC) from baseline at Week 96 or early termination
3.2. New/newly enlarged T2 lesion count (compared with baseline MRI scan) at Week 96 or early termination
4. Quality of Life assessment:
4.1. Multiple Sclerosis Quality of Life (MSQOL)-54 instrument from baseline up to Week 96
4.2. Modified Fatigue Impact Scale (MFIS) from baseline up to Week 96
4.3. Hamilton Depression Rating Scale (HAM-D) from baseline up to Week 96
4.4. Disability Impact Profile (DIP) from baseline up to Week 96
5. Relapses measured using patient records:
5.1. Occurrence of new or worsening neurological symptoms attributable to MS
5.2. Symptoms persisting for >24 hours
5.3. Symptoms not attributable to confounding clinical factors (e.g., fever, infection, injury, adverse reactions to medications)
5.4. Symptoms immediately preceded by a stable or improving neurological state for at least 30 days
5.5. Symptoms accompanied by objective neurological worsening consistent with an increase of at least half a step on the EDSS scale
6. Biomarker(s):
6.1. Comparison of serum Neurofilament Light Chain (NfL) and Glial Fibrillary Acidic Protein

(GFAP) levels at Baseline and Week 96 or early termination (only if patient discontinues after Week 48 and more than 24 weeks have elapsed since last test) These biomarkers are to be tested in a subgroup of 200 patients of pre-selected sites

Completion date
01/06/2026

Eligibility

Key inclusion criteria
1. Patients with either primary progressive or secondary progressive multiple sclerosis with onset of symptoms at least five years before inclusion and with no relapse diagnosed according to the 2017 revised McDonald's criteria at least two years before screening
2. Patients with Expanded Disability Status Scale (EDSS) score between 3.0 to 6.0 (both inclusive) at screening and baseline
3. Patients with an EDSS score progression ≥1 point with no improvement during 2 years before screening
4. Absence of T1 Gadolinium-enhancing brain lesions at baseline as measured by MRI at screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Patients suffering from a disease other than MS that would better explain the patient's neurological clinical signs and symptoms and/or MRI lesions observed at screening
2. Inability to complete screening MRI (contraindications for MRI) and/or any known allergy or hypersensitivity or any contra-indication to gadolinium macrocyclic
3. Patients treated with other disease modifying treatments in the time frames and conditions mentioned under previous treatment wash out period, assessed at baseline
4. Patients with lymphocytes <1.0 × 10^9/L at screening and at baseline

Date of first enrolment
31/03/2022

Date of final enrolment
01/06/2026

Locations

Countries of recruitment
United Kingdom

England

Argentina

Belgium

France

Germany

Greece

Hungary

Italy

Netherlands

Norway

Poland

Portugal

Romania

Russian Federation

South Africa

Spain

Sweden

Ukraine

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Study participating centre
Salford Royal Hospital
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Sponsor information

Organisation
Dokumeds

Funder(s)

Funder type
Industry

Funder Name
AB Science

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

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?
HRA research summary			28/06/2023	No	No