ForPatients
by Roche

Multiple Sclerosis (MS)

A clinical trial to look at how safe different doses of RO7121932 are in people with multiple sclerosis and how the body processes RO7121932

A Study to Investigate the Safety, Tolerability, and Processing by the Body of Intravenous and Subcutaneous RO7121932 in Participants With Multiple Sclerosis.

Trial Status	Trial Runs In	Trial Identifier
Recruiting	12 Countries	NCT05704361 2020-004122-33 BP42230

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

Official Title: A Multiple-Center, Non-randomized, Open-label, Adaptive, Single-Ascending Dose (Part 1 and Part 2) and Multiple-Ascending Dose (Part 3) Parallel, Phase IB Study to Investigate the Safety, Tolerability, Immunogenicity, Pharmacokinetics, and Pharmacodynamics of RO7121932 Following Intravenous (Part 1) and Subcutaneous Administration (Parts 2 and 3) in Participants With Multiple Sclerosis

Trial Summary:

The primary purpose of the study is to evaluate the safety and tolerability of single ascending intravenous (IV) (Part 1) and subcutaneous (SC) (Part 2) doses of RO7121932 and multiple ascending SC (Part 3) doses of RO7121932 in participants with multiple sclerosis (MS).

Hoffmann-La Roche Sponsor	**Phase 1** Phase

NCT05704361 2020-004122-33 BP42230
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years & # 65 Years	No

1. Why is the B-Shuttle clinical trial needed?

Multiple sclerosis (MS) is a health condition in which the immune system (the body's natural defence) attacks the protective covering of nerve fibres in the brain and spinal cord. This leads to communication problems between the brain and the rest of the body. People with MS may feel tired or weak, have difficulty walking or lose their balance. They may also find it difficult to control urination or bowel movements. People with MS may have numb or tingling sensations and blurred vision. Gradual loss of brain functions like thinking, remembering and reasoning to the point where it interferes with daily activities is also a symptom of MS.

The most common type of MS is 'relapsing-remitting' MS (RRMS). This form of MS has periods of getting worse and getting better. A relapse is the return of signs, symptoms, or a disease after they have improved for a while. Progressive multiple sclerosis (PMS) is another form of MS where symptoms steadily worsen. PMS can worsen very quickly. People with PMS can have primary PMS (PPMS) – they have progressive symptoms from the start. Or, secondary PMS (SPMS) – they have PMS that develops from RRMS. Worsening disability in PMS could be due to nerve damage in the brain.

Treatments for MS include:

- Medicines that reduce inflammation, known as steroids, to treat relapses
- Treatment of MS symptoms
- Disease-modifying therapies (DMTs) to prevent MS relapses and maintain body functions

Treatment with DMTs can reduce MS activity. But DMTs find it difficult to get into the brain due to the blood-brain barrier. This is a protective barrier in the brain vessels that stops certain things going from the blood into the brain. New treatments for MS are needed that can pass through the blood-brain barrier and stop nerve damage in the brain.

RO7121932 is an experimental drug. This means health authorities have not approved it for treating MS. RO7121932 uses a 'brain shuttle technology' that allows the drug to pass through the blood-brain barrier. This clinical trial aims to test how safe and tolerable RO7121932 is at different doses in people with MS when given as a drip into a vein or an injection under the skin. It also aims to understand what happens to RO7121932 once it is in the body and what effects, good or bad, it has.

2. How does the B-Shuttle clinical trial work?

This clinical trial is recruiting people with RRMS, PPMS and SPMS. People who take part in this clinical trial (participants) will be given the clinical trial treatment RO7121932. They will need to stay in the hospital overnight after being given RO7121932 on Day 1. The clinical trial doctor will see them regularly. These hospital visits will include medical checks to see how the participant responds to treatment and any unwanted effects they may have. Some visits and tests may be done by a mobile nurse at the participants' home if they agree to it. Participants will have a final follow-up visit after about 6 months of

completing clinical trial treatment, during which the clinical trial doctor will check on the participant's wellbeing. Total time of participation in the clinical trial will be about 7 or 8 months. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the B-Shuttle clinical trial?

The main clinical trial endpoint (the main result measured in the trial) is the number and seriousness of any unwanted effects during treatment and the 6-month follow-up period.

The other clinical trial endpoints include:

- How RO7121932 gets to different parts of the body, and how the body changes and gets rid of it
- How RO7121932 affects the immune system

4. Who can take part in this clinical trial?

People aged 18 to 65 years old with RRMS, PPMS and SPMS can take part in this trial. However, they cannot be currently treated with DMTs and cannot have had very recent MS activity. This means they have not had a relapse within 3 months of joining the trial. They can also only have had 1 relapse within the past year. Or, they will have few new or enlarging lesions in the brain on a recent scan. Participants can continue having physiotherapy or taking any treatments for MS symptoms that they have already started.

People may not be able to take part in this trial if they have recently received certain treatments such as B-cell therapies. Or, they have certain medical conditions that affect the brain or spinal cord (known as neurological conditions). People who have infections or have had cancer within the last 10 years also cannot take part. Neither can pregnant or breastfeeding people. They also cannot join if they plan to become pregnant during the trial.

5. What treatment will participants be given in this clinical trial?

This clinical trial is split into 3 parts. The part of the trial participants will join will depend on when they start the trial. Participants will be given either:

- **Part 1:** RO7121932, given once, as a drip into a vein, OR
- **Part 2:** RO7121932, given once, as an injection under the skin, OR
- **Part 3:** RO7121932, given as an injection under the skin once a week OR as a drip into a vein for the first dose then as an injection under the skin once a week

If participants have a relapse or their MS becomes active again as shown on MRI scans, they may be offered approved immunotherapy treatment if the clinical trial doctor believes this will benefit them. This is an open-label trial. This means that everyone involved,

including the participant and the clinical trial doctor, will know the clinical trial treatment (RO7121932) the participant has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of MS. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drug Participants may have unwanted effects from the drug used in this clinical trial. Unwanted effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

Participants will be told about the known side effects of RO7121932 and, where relevant, potential side effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known unwanted effects of drips into a vein and injections under the skin.

Potential benefits associated with the clinical trial Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Expanded Disability Status Scale (EDSS) score #7.0 at Screening
- Participants with relapsing multiple sclerosis (RMS) or progressive multiple sclerosis (PMS) who fulfil international panel criteria for diagnosis (McDonald 2017 criteria)
- Participants not treated with any approved MS treatment at Screening and not planning to start on any MS therapy during the study (including follow-up)
- Female participants must practice abstinence or otherwise use contraception

Exclusion Criteria:

- Evidence of clinical disease activity as defined by any clinical relapse within 3 months prior to screening, or by >1 clinical relapse within 12 months prior to screening
- Evidence of magnetic resonance imaging (MRI) activity as defined by the presence of # 1 Gadolinium-enhancing T1 lesion in the screening MRI scan or by # 4 new or enlarging T2 lesions in the screening scan as compared to a reference scan
- Participants who have active progressive multifocal leukoencephalopathy (PML), have had confirmed PML, or have a high degree of suspicion for PML

- Known presence of other neurological disorders that may mimic MS including but not limited to: neuromyelitis optica spectrum disease, Lyme disease, untreated Vitamin B12 deficiency, neurosarcoidosis, cerebrovascular disorders, and untreated hypothyroidism
- Known active or uncontrolled bacterial, viral, fungal, mycobacterial infection or other infection, excluding fungal infection of nail beds, including participants exhibiting symptoms consistent with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) within 6 weeks prior to Day 1
- Participants with a current diagnosis of epilepsy
- Clinically significant cardiac, metabolic, hematologic, hepatic, immunologic, urologic, endocrinologic, neurologic, pulmonary, psychiatric, dermatologic, allergic, renal, or other major diseases
- History of cancer, including hematologic malignancy and solid tumors, within 10 years of screening. Basal or squamous cell carcinoma of the skin that has been excised and is considered cured and in situ carcinoma of the cervix treated with apparent success by curative therapy >1 year prior to screening is not exclusionary
- Any concomitant disease that may require treatment with systemic corticosteroids or immunosuppressants during course of the study
- History of currently active primary or secondary (non-drug-related) immunodeficiency
- History of hypersensitivity to biologic agents or any of the excipients in the formulation
- Only for cohorts where CSF samples are planned to be collected: Participants with a history of spinal cord compression, raised intra-cerebral pressure, clinically significant vertebral joint pathology or any other current abnormalities in the lumbar region which could prevent the lumbar puncture procedure.

Prior/Concomitant Therapy:

- Treatment with any approved MS treatment at Screening. Participants may become eligible after completion of a washout period prior to acquiring any screening laboratory tests but should not be withdrawn from therapies for the sole purpose of meeting eligibility for the trial
- Previous treatment with RO7121932, alemtuzumab, cladribine, mitoxantrone, cyclophosphamide, total body irradiation, bone marrow transplantation, and hematopoietic stem cell transplantation. For the USA only, previous treatment with daclizumab
- Previous treatment with anti-CD20 B-cell-depleting therapies (e.g., rituximab, ocrelizumab, or ofatumumab)
- <12 months prior to acquiring any screening laboratory tests, * #12 months prior to acquiring any screening laboratory tests, if B-cells are outside the normal range, or not back to individual baseline ± 20% (if data are available), * If discontinuation of a prior B-cell depletion therapy was motivated by safety reasons
- Current or prior treatment with natalizumab (if <24 months prior to acquiring any screening laboratory tests)

Prior/Concurrent Clinical Study Experience:

- Participation in an investigational drug medicinal product or medical device study within 30 days before Screening or within five times the pharmacodynamic (PD) or pharmacokinetic (PK) half-life (if known), whichever is longer

Diagnostic Assessments:

- Positive result on human immunodeficiency virus (HIV1) and HIV2, hepatitis C, or hepatitis B
- Participants with suicidal ideation or behavior within 6 months prior to Screening or participants who, in the Investigator's judgment, pose a suicidal or homicidal risk
- Vaccination with a live or live-attenuated vaccine within 6 weeks prior to Day 1