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A study to investigate the safety, tolerability, and processing by the body of intravenous RO7121932 in patients with multiple sclerosis

Submission date
01/04/2021

Recruitment status
No longer recruiting

Registration date
08/06/2021

Overall study status
Completed

Last Edited
05/12/2023

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
This is the first study where the drug RO7121932 will be given to humans. All participants will be people living with multiple sclerosis (MS), a long-term disease that attacks the central nervous system, affecting the brain, spinal cord, and optic nerves. The aims of this study are to test the safety of RO7121932 at different dose levels; determine how well it is tolerated by the participants; measure how the body absorbs, distributes, and gets rid of it (this is called pharmacokinetics); and find out what effects, good or bad, RO7121932 has on the participant (this is called pharmacodynamics).

Who can participate?
People aged 18 to 65 living with MS

What does the study involve?
All participants in this study will receive a single dose of RO7121932 in the morning of Day 1, which is given by an intravenous infusion (via a tube linked to a small needle into the vein). About 42 participants are expected to be enrolled in this study with the maximum number of participants not exceeding 63. At each new dose level, one participant will be dosed on Day 1, and at least 5 participants will be dosed no earlier than 36 hours thereafter. Each dose level will be reviewed and the next, higher dose will be determined based on the data available. An optional exit interview will be conducted via phone or a web-based questionnaire any time during the follow-up period to gather feedback on the study experience. Certain study assessments may be performed at the participant's home.

What are the possible benefits and risks of participating?
There is currently no clinical experience with RO7121932. This first in human study is being conducted in patients with MS. No or very limited benefit to the participants enrolled in this study is expected.

Where is the study run from?
Hospitals in Belgium, Germany, Israel, Italy, Poland, Portugal and the United States

When is the study starting and how long is it expected to run for?
November 2020 to January 2025

Who is funding the study?
Genentech, Inc (USA)

Who is the main contact?
global-roche-genentech-trials@gene.com

Study website
https://forpatients.roche.com/en/trials/autoimmune-disorder/multiple-sclerosis/a-study-to-investigate-the-safety--tolerability--and-pr-15846.html

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
2020-004122-33

IRAS number

ClinicalTrials.gov number
NCT05704361

Secondary identifying numbers
BP42230

Study information

Scientific Title
A multiple-center, non-randomized, open-label, adaptive, single ascending dose, Phase I study to investigate the safety, tolerability, immunogenicity, pharmacokinetics, and pharmacodynamics of RO7121932 following intravenous administration in patients with multiple sclerosis

Study objectives
To investigate the safety, tolerability, and processing by the body of intravenous RO7121932 in patients with multiple sclerosis

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/04/2021, Universitair Ziekenhuis Gent - Commissie voor medische ethiek (Ingang 75, route 7522 - C. Heymanslaan 10, 9000 Gent, Belgium; +32 (0)9 332 26 88; ethisch. comite@uzgent.be), ref: BC-09646

Study design
Multiple-center non-randomized open-label study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not applicable

Health condition(s) or problem(s) studied
Multiple sclerosis, brain shuttle

Interventions
All participants in this study will receive a single dose of RO7121932 in the morning of day 1, which is given by an intravenous infusion (via a tube linked to a small needle into the vein).

Six dose levels are planned initially:
Cohort 1 – 7 mg RO7121932 (starting dose)
Cohort 2 – 20 mg RO7121932
Cohort 3 – 70 mg RO7121932
Cohort 4 – 200 mg RO7121932
Cohort 5 – 700 mg RO7121932
Cohort 6 – 2000 mg RO7121932

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
RO7121932

Primary outcome measure
1. Incidence, severity, seriousness, and causal relationship of adverse events (AEs): AEs taken from participant's medical records throughout the course of the study (baseline to day 169/early termination)
2. Incidence of abnormal laboratory findings: clinical laboratory safety assessments measured by the evaluation of blood and urine tests from baseline to day 169/early termination
3. Incidence of abnormal vital signs and electrocardiogram (ECG) parameters: blood pressure and pulse rate measured by an automated device and ECG abnormalities measured by 12-lead ECG from baseline to day 169/early termination
4. Suicidal risk monitoring measured using the Columbia-Suicide Severity Rating Scale at baseline, day 3, day 8, day 29, day 85 and day 169/early termination

Secondary outcome measures
1. Serum PK parameters of RO7121932 measured by specific and validated methods on serum samples taken at predose, 0.5, 1 (or end of infusion), 2, 3 (or end of infusion), 8 h on day 1, on day 2, day 3, day 5, day 8, day 15, day 22, day 29, day 57, day 85, day 113, and day 169/early termination
2. CSF concentration of RO7121932 (Cohort 5 and 6 only) measured by specific and validated methods on 1 CSF sample taken between day -7 and day -1, prior to dosing and a postdose CSF sample taken anytime from day 2 to day 169. A third optional CSF sample (if consented) is also taken from day 2 to day 169
3. Incidence of anti-RO7121932 antibodies measured using validated screening, confirmatory, and titer assays on serum samples taken at predose, day 8, day 22, day 29, day 57, day 85 and day 169/early termination
4. PD parameters:
4.1. B cells measured by flow cytometry from blood samples taken at screening, predose on day 1, day 2, day 8, day 22, day 57, day 85 and day 169/early termination
4.2. B cells (Cohort 5 and 6 only) measured by flow cytometry from 1 CSF sample taken between day -7 and day -1, prior to dosing and a postdose CSF sample taken anytime from day 2 to day 169. A third optional CSF sample (if consented) is also taken from day 2 to day 169

Overall study start date
20/11/2020

Completion date
16/01/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 16/05/2022:
1. Ability to provide, informed consent, to be able to follow the SoA and to comply with the study protocol according to the International Council on Harmonisation and local regulations
2. 18 to 65 years, inclusive, at time of signing Informed Consent Form
3. Fluent in the language of the Investigator and study staff, and able to communicate with the study staff
4. Expanded Disability Status Scale (EDSS) score ≤7.0 at Screening
5. Non-active patients with relapsing MS or progressive MS who fulfilled international panel

criteria for diagnosis, as per the revised McDonald 2017 criteria (Thompson 2018) and the Lublin criteria (Lublin et al. 2014; Lublin et al 2020) (see also exclusion criterion 1)
6. Patients not treated with any approved MS treatment at Screening and not planning to start on any MS therapy during the study (including follow-up)
7. Female participants must practice abstinence or otherwise use contraception

Previous inclusion criteria:
1. Ability to provide written, informed consent, to be able to follow the SoA and to comply with the study protocol according to the International Council on Harmonisation and local regulations
2. 18 to 55 years, inclusive, at time of signing Informed Consent Form
3. Fluent in the language of the Investigator and study staff, and able to communicate with the study staff
4. Expanded Disability Status Scale (EDSS) score ≤6.0 at Screening
5. Non-active patients with relapsing MS (RMS) or progressive MS (PMS) who fulfilled international panel criteria for diagnosis, as per the revised McDonald 2017 criteria (Thompson 2018) and the Lublin criteria (Lublin et al. 2014) (see also exclusion criteria 1 and 2)
6. Patients not treated with any approved MS treatment at Screening and not planning to start on any MS therapy during the study (including follow-up)
7. Male and female participants must practice abstinence or otherwise use contraception

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
63

Key exclusion criteria
Current exclusion criteria as of 16/05/2022:
1. Any signs of disease activity suggested clinically (relapse) or by magnetic resonance imaging (MRI) (gadolinium [Gd]-enhancing T1 lesions or new or enlarging T2 lesions) within 12 months prior to Screening
2. Participants who have active progressive multifocal leukoencephalopathy (PML), have had confirmed PML, or have a high degree of suspicion for PML
3. 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
4. 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
Note: Participants who tested positive for SARS-CoV-2 in the past but are without any current symptoms related to coronavirus disease 2019 should be carefully and comprehensively

evaluated as per usual medical practice and institutional guidance before enrollment. The Investigator should assess the benefit/risk ratio for each participant with a history of SARS-CoV2 infection; enrollment has to be discussed with both the participant and the Sponsor. For participants not yet fully immunized against SARS-CoV-2, COVID-19 testing should be performed up to 48 hours prior to study drug administration, per local institutional guidelines, if required per local regulations.
5. Participants with a current diagnosis of epilepsy
6. Clinically significant cardiac, metabolic, hematologic, hepatic, immunologic, urologic, endocrinologic, neurologic, pulmonary, psychiatric, dermatologic, allergic, renal, or other major diseases that in the Investigator's judgment may affect the interpretation of study results or patient safety
7. 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.
8. Any concomitant disease that may require treatment with systemic corticosteroids or immunosuppressants during the course of the study
9. History of currently active primary or secondary (non-drug-related) immunodeficiency
10. History of hypersensitivity to biologic agents or any of the excipients in the formulation.
11. Cohorts 5 and 6 and later cohorts, as appropriate: 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 (skin infection, develop abnormalities in lower spine, etc) which could prevent the lumbar puncture procedure

Prior/Concomitant Therapy:
12. Treatment with any approved MS treatment at Screening. Participants may become eligible after completion of a washout period prior to Screening but should not be withdrawn from therapies for the sole purpose of meeting eligibility for the trial. Justification for withdrawal from medication must be documented.
13. Previous treatment with any other immunomodulatory or immunosuppressive medication not already listed above without appropriate washout as described in the applicable local label (washout to be completed prior to Screening). If the washout requirements are not described in the applicable local label, then the washout period must be at least 30 days before Screening or within five times the PD or PK half-life (if known), whichever is longer. The washout periods can be discussed between the Investigator and Sponsor.
14. Previous treatment with alemtuzumab, daclizumab, cladribine, mitoxantrone, cyclophosphamide, total body irradiation, bone marrow transplantation, and hematopoietic stem cell transplantation.
15. Previous treatment with anti-CD20 B-cell-depleting therapies (e.g., rituximab, ocrelizumab, or ofatumumab)
a. <12 months prior to Screening,
b. ≥12 months prior to Screening, if B-cells are outside the normal range, or not back to individual baseline ± 20% (if data are available),
c. if discontinuation of a prior B-cell depletion therapy was motivated by safety reasons.
16. Current or prior treatment with natalizumab (if <24 months prior to Screening).
17. Treatment with any investigational agent within 24 weeks prior to Screening or 5 PK or PD half-lives of the investigational drug (whichever is longer) for any medical indication or treatment with any experimental procedure for MS (e.g., treatment for chronic cerebrospinal venous insufficiency)
18. Treatment with Botox for limb spasticity within 24 weeks before Screening
19. Systemic corticosteroid therapy within 4 weeks prior to Screening. Intrathecal corticosteroid therapy within 24 weeks prior to Screening.

Prior/Concurrent Clinical Study Experience:
20. Participation in an investigational drug medicinal product or medical device study within 30 days before Screening or within five times the PD or PK half-life (if known), whichever is longer

Diagnostic Assessments:
21. Positive result on HIV1 and HIV2, hepatitis C, or hepatitis B
22. Positive test for drugs of abuse or alcohol
23. Lymphocyte count <1000/μL, serum IgG <4.6 g/L, and absolute neutrophil count <1500/μl at Screening.
24. Confirmed (may use an average of ≥2 blood pressure measurements) abnormal blood pressure at Screening: supine systolic blood pressure <90 mm Hg or >140 mm Hg or diastolic blood pressure <45 mm Hg or >90 mmHg
25. Pulse rate (may use an average of ≥2 pulse measurements) > 90 beats per minute or <45 beats per minute (at Screening only)
26. History or presence of clinically significant ECG abnormalities (e.g., PR interval >220 ms, QTcF >450 ms in male participants/QTcF >470 ms in female participants (average of triplicates to be considered) or cardiovascular disease (e.g., cardiac insufficiency, coronary artery disease, cardiomyopathy, congestive heart failure, family history of congenital long QT syndrome, family history of sudden death) at Screening
27. Clinically significant abnormalities (as judged by the Investigator) in laboratory test results (including hematology, blood chemistry and urinalysis), not linked to the participant's MS disease. Platelet count, hemoglobin, hematocrit, and reticulocytes (absolute count) must be within the reference range of the laboratory performing the assessment at Screening
28. Impaired hepatic function as indicated by Screening aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 1.5 × the upper limit of normal (ULN) or abnormal total bilirubin unless due to Gilbert disease
29. 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
30. History of drug or alcohol abuse within the past year
31. Vaccination with a live or live-attenuated vaccine within 6 weeks prior to Day 1. Influenza and /or COVID-19 vaccination is permitted if the inactivated vaccine formulation is administered. Investigators are advised to review the immunization status of participants who are considered for treatment with RO7121932 and follow local/national guidance for adult vaccination against infectious disease
32. Contraindications for, or intolerance to oral or IV corticosteroids, antihistamines, including uncontrolled psychosis for corticosteroids or closed-angle glaucoma for antihistamines
33. Any contraindications for MRI scans (including but not limited to claustrophobia, pacemaker, artificial heart valves, cochlear implants, presence of foreign metal objects in head or body, intracranial vascular clips, etc.) or any brain/head abnormalities restricting MRI eligibility
34. Lack of peripheral venous access
35. Participants who have donated over 450 ml of blood or blood products or had significant blood loss within 3 months prior to Screening

Previous exclusion criteria:
1. Participants with an MS relapse that has occurred within 24 weeks prior to Screening, or the participant has not stabilized from a previous relapse at time of Screening
2. Signs of magnetic resonance imaging (MRI) activity (gadolinium [Gd]-enhancing T1 lesions or new or enlarging T2 lesions), as judged from an MRI scan taken within 3 months prior to Screening or taken during Screening, when compared with a previous MRI scan (not older than 12 months)
3. Participants who have active progressive multifocal leukoencephalopathy (PML), have had

confirmed PML, or have a high degree of suspicion for PML
4. 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
5. 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
Note: Participants who tested positive for SARS-CoV-2 in the past but are without any current symptoms related to coronavirus disease 2019 should be carefully and comprehensively evaluated as per usual medical practice and institutional guidance before enrollment. The Investigator should assess the benefit/risk ratio for each participant with a history of SARS-CoV-2 infection; enrollment has to be discussed with both the participant and the Sponsor
6. Participants with a current diagnosis of epilepsy
7. Clinically significant cardiac, metabolic, hematologic, hepatic, immunologic, urologic, endocrinologic, neurologic, pulmonary, psychiatric, dermatologic, psychiatric, allergic, renal or other major diseases that in the Investigator's judgment may affect the interpretation of study results or patient safety
8. Any concomitant disease that may require treatment with systemic corticosteroids or immunosuppressants during the course of the study
9. History of currently active primary or secondary (non-drug-related) immunodeficiency
10. Cohorts 5 and 6 and later cohorts, as appropriate: 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 (skin infection, develop abnormalities in lower spine, etc) which could prevent the lumbar puncture procedure

Prior/Concomitant Therapy:
11. Treatment with any approved MS treatment at Screening. Participants treated with interferon, glatiramer acetate, and dimethyl fumarate may become eligible after completion of a 14-day washout period prior to Screening with peripheral total white blood cell count being in the normal range.
12. Previous treatment with B cell-depleting therapies (e.g., rituximab, ocrelizumab, or ofatumumab), alemtuzumab, mitoxantrone, total body irradiation, bone marrow transplantation and hematopoietic stem cell transplantation.
13. Treatment with cladribine within 12 months prior to enrollment or current or prior treatment with natalizumab.
14. Treatment with any investigational agent within 24 weeks prior to Screening or 5 PK or PD half-lives of the investigational drug (whichever is longer) for any medical indication or treatment with any experimental procedure for MS (e.g., treatment for chronic cerebrospinal venous insufficiency)
15. Treatment with Botox for limb spasticity within 24 weeks before Screening
16. Systemic corticosteroid therapy within 4 weeks prior to Screening

Prior/Concurrent Clinical Study Experience:
17. Participation in an investigational drug medicinal product or medical device study within 30 days before Screening or within five times the PD or PK half-life (if known), whichever is longer

Diagnostic Assessments:
18. Positive result on HIV1 and HIV2, Hepatitis C, or Hepatitis B
19. Positive test for drugs of abuse or alcohol
20. Lymphocyte count <1000/μL, serum IgG <4.6 g/L, and absolute neutrophil count <1500/μl
21. Confirmed (may use an average of ≥2 blood pressure measurements) abnormal blood

pressure at Screening: supine systolic blood pressure <90 mm Hg or >140 mm Hg or diastolic blood pressure <45 mm Hg or >90 mmHg
22. Pulse rate (may use an average of ≥2 pulse measurements) > 90 beats per minute or <45 beats per minute (at Screening only)
23. History or presence of clinically significant ECG abnormalities (e.g., PR interval >220 ms, QTcF >450 ms in male participants/QTcF >470 ms in female participants (average of triplicates to be considered) or cardiovascular disease (e.g., cardiac insufficiency, coronary artery disease, cardiomyopathy, congestive heart failure, family history of congenital long QT syndrome, family history of sudden death) at Screening
24. Clinically significant abnormalities (as judged by the Investigator) in laboratory test results (including hematology, blood chemistry and urinalysis), not linked to the participant's MS disease. Hemoglobin, hematocrit, and reticulocytes (absolute count) must be within the reference range of the laboratory performing the assessment at Screening
25. Impaired hepatic function as indicated by Screening aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 1.5 × the upper limit of normal (ULN) or abnormal total bilirubin unless due to Gilbert disease
26. 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
27. History of drug or alcohol abuse within the past year
28. Vaccination with a live or live-attenuated vaccine within 6 weeks prior to Day 1. Influenza and /or Coronavirus disease 2019 vaccination is permitted if the inactivated vaccine formulation is administered. Investigators are advised to review the immunization status of participants who are considered for treatment with RO7121932 and follow local/national guidance for adult vaccination against infectious disease
29. Contraindications for, or intolerance to oral or IV corticosteroids, antihistamines, including uncontrolled psychosis for corticosteroids or closed-angle glaucoma for antihistamines
30. Any contraindications for MRI scans (including but not limited to claustrophobia, pacemaker, artificial heart valves, cochlear implants, presence of foreign metal objects in head or body, intracranial vascular clips, etc.) or any brain/head abnormalities restricting MRI eligibility
31. Lack of peripheral venous access
32. Participants who have donated over 450 ml of blood or blood products or had significant blood loss within 3 months prior to Screening

Date of first enrolment
11/08/2021

Date of final enrolment
31/07/2024

Locations

Countries of recruitment
Belgium

Germany

Israel

Italy

Poland

Portugal

United States of America

Study participating centre
Instytut Psychiatrii i Neurologii II Klinika Neurologiczna
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre

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Sponsor type
Industry

Website
https://www.roche.com/about/business/roche_worldwide.htm

Funder(s)

Funder type
Industry

Funder Name
Genentech, Inc

Results and Publications

Publication and dissemination plan
The publication and dissemination plan is unknown. No additional study documents will be made available.

Intention to publish date
08/01/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement for Phase I studies.

IPD sharing plan summary

Not expected to be made available