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A study to investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of selnofast in participants with early idiopathic Parkinson's disease

Submission date
07/12/2021

Recruitment status
No longer recruiting

Registration date
29/04/2022

Overall study status
Completed

Last Edited
26/07/2024

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:
Parkinson’s disease (PD) is a progressive and incurable disease that affects the nervous system. It is caused by the loss of brain cells that produce dopamine, a chemical that helps brain cells communicate and control movement. The main symptoms include decreased mobility, rigidity or stiffness of arms, legs and trunk, and resting tremors (shaking that occurs at rest). Evidence suggests that people with PD may have increased inflammation (swelling) in the brain. A protein called NLRP3 is thought to play a key role in this inflammatory process. Selnoflast is a new drug that has been developed to slow the progression of disease in people with early PD. Selnoflast acts by blocking NLRP3, which might lower the inflammation in the brain. Health authorities have not yet approved selnoflast for the treatment of PD or any other disease. The main purpose of this study is:
-To determine how safe and tolerable selnoflast is when compared to a placebo (medicine without an active ingredient)
-To determine how selnoflast is absorbed, distributed and, eventually eliminated from the body
-To assess the effect of selnoflast on the inflammation in the brain using certain scans called the TSO-PET scans

Who can participate?
People aged between 40 to 85 years with PD.

What does the study involve?
Participants may be asked to be in the study for approximately 100 days. This includes: -
Screening Period of up to 60 days where tests will be done to check if the participants are eligible to take part in the study. Participants may have to visit the clinic approximately 3 times during the Screening Period.
Baseline Period of up to 3 days before the start of study wherein participants will be contacted over the phone to collect details about other medicines and changes to their health and life. MRI and TSPO PET scans will also be done at this time. The participants will have to report to a

dedicated external PET center for the scans.
Treatment Period of approximately 28 days where participants will have to report 5 times to the clinic and 1 time to a dedicated external PET centre for tests, assessments, and procedures in addition to taking the study medication twice a day.
Follow-up Period where participants will have a check-up approximately 14 days after the last study treatment administration.
Participants will be placed in one of the following treatment groups:
Group 1 will receive selnoflast, given as capsules for about 28 days.
Group 2 will receive a placebo, given as capsules for about 28 days.

What are the possible benefits and risks of participating?
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.
Participants may have side effects from the drugs or procedures used in this study that can be mild to severe or even life-threatening in nature, and they can vary from person to person.
Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

Where is the study run from?
Roche (Switzerland)

When is the study starting and how long is it expected to run for?
September 2021 to July 2024

Who is funding the study?
Roche (Switzerland)

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

Contact information

Type(s)
Public

Contact name
Dr Clinical Trials

Contact details
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Additional identifiers

Clinical Trials Information System (CTIS)

2023-504412-14-00

Integrated Research Application System (IRAS)
307220

ClinicalTrials.gov (NCT)
NCT05924243

Protocol serial number
BP43176, CPMS 50823, IRAS 307220

Study information

Scientific Title
A phase 1b, adaptive, multi-center, randomized, double blind, placebo-controlled, parallel design study to investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of selnofast in participants with early idiopathic Parkinson's disease

Study objectives
Current study hypothesis as of 24/07/2023:

The aim of the study is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of selnoflast in participants with early idiopathic Parkinson’s disease (PD).

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Previous study hypothesis:

The aim of the study is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of RO7486967 in participants with early idiopathic Parkinson’s disease (PD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/04/2021, WCG IRB (1019 39th Avenue, SE Suite 120 Puyallup, WA 98374, USA; +1 855-818-2289; clientservices@wcgirb.com), ref: 20215051

Study design
Phase 1b adaptive multicentre double-blind randomized placebo-controlled parallel design study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Parkinson’s disease

Interventions
Current interventions as of 24/07/2023:

Selnoflast: Participants will receive selnoflast capsules for 28 days.
Placebo: Participants will receive a matching placebo to selnoflast capsules for 28 days.
Randomisation is done using an Interactive Voice/Web Response System (IxRS)

Previous interventions:

RO7486967: Participants will receive RO7486967 capsules, 200 mg, orally, twice daily, for 28 days.
Placebo: Participants will receive a matching placebo to RO7486967 capsules, orally, twice daily, for 28 days.
Randomisation is done using an Interactive Voice/Web Response System (IxRS)

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
1. Percentage of Participants with Adverse Events, Serious Adverse Events and Severity per National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE V5.0) from Screening up to Approximately 6 Weeks
2. Percentage of Participants with Abnormal Laboratory Findings in Blood and Urine from Screening up to Approximately 6 Weeks
3. Percentage of Participants with Abnormal Vital Signs and ECG Parameters Using Manual Techniques and Instrument Respectively from Screening up to Approximately 6 Weeks
4. Change from Baseline in Columbia Suicide Severity Rating Scale (C-SSRS) Using Interview-Based Instrument from Screening up to Approximately 6 Weeks

Key secondary outcome(s))
Current secondary outcome measures as of 24/07/2023:

1. Time to Maximum Concentration of Selnoflast using Blood Samples on Days 1, 15 and 28
2. Area Under the Curve (AUC) of Selnoflast using Blood samples on Days 1, 15 and 28
3. Maximum Concentration (Cmax) of Selnoflast using Blood Samples on Days 1, 15 and 28
4. Change from Baseline in Parametric Bindings of [18F]-DPA-714 in Different Brain Areas Using TSPO positron emission tomography [PET] Imaging from Baseline to Day 25

Previous secondary outcome measures:

1. Serum Concentration of RO7486967 Using Blood and Cerebrospinal Fluid (CSF) Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
2. Area Under the Curve 0-6 hr [AUC(0-6h)] of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
3. AUC (12h) of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
4. Maximum Concentration (Cmax) of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
5. Time to Achieve Maximum Concentration (Tmax) of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
6. Terminal Half-Life (t1/2) of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
7. Total Clearance (CL/F) of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
8. Volume of Distribution at Steady-State (Vss/F) of RO7486967 Using Blood and CSF Samples at Predose, 0.5 h, 1 h, 2 h, 4 h, 6 h on Days 1, 15 and 28
9. Change from Baseline in Parametric Bindings of [18F]-DPA-714 in Different Brain Areas Using TSPO positron emission tomography [PET] Imaging at Day 25

Completion date
18/07/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/07/2023:

1. Male or post-menopausal female
2. Diagnosis of clinically probable idiopathic PD based on movement disorder society (MDS) criteria with bradykinesia plus one of the other cardinal signs of PD (resting tremor, rigidity)
3. A time from diagnosis of PD of at least 3 to maximum 60 months (5 years) at screening
4. Modified Hoehn and Yahr (H&Y) Stage ≤2.5 (in ON state)
5. Dopaminergic imaging consistent with dopamine transporter deficit
6. “High-affinity binder” or “mixed-affinity binder” for TSPO
7. Either treatment naïve or treatment with symptomatic PD therapy (levodopa and/or pramipexole, ropinirole, rotigotine) given for at least 90 days, with stable doses for at least 30 days prior to the first dose
8. No anticipated changes in PD therapy throughout the study duration
9. SARS-CoV-2 vaccination completed at least 60 days prior to the first dose.

Previous inclusion criteria:

1. Males and post-menopausal females aged 50-85 years at the time of signing Informed Consent Form (ICF)
2. Diagnosis of clinically probable idiopathic PD based on Movement Disorder Society (MDS) criteria with bradykinesia plus one of the other cardinal signs of PD (resting tremor, rigidity), at least 3 to maximum 36 months prior to screening
3. No motor complications, assessed by a score of 0 on the Movement Disorder Society-Unified

Parkinson's Disease Rating Scale (MDS-UPDRS) Part IV at screening (for participants on levodopa treatment)
4. Modified Hoehn and Yahr (H&Y) Stage ≤2.5 (for participants on levodopa treatment in ON state)
5. Dopaminergic imaging is consistent with dopamine transporter deficit. A previously performed dopaminergic imaging scan (e.g., DAT-SPECT or FDOPA-PET) is also accepted if it was indicative of a dopaminergic deficit typical of Parkinson’s disease
6. “High-affinity binder” or “mixed-affinity binder” for TSPO, as confirmed by prospective genotyping of TSPO polymorphism during screening
7. Able to swallow capsules whole
8. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination completed at least 60 days prior to the first dose. Individual vaccination complete status to be defined as per local regulations at the time of screening
9. Agree to reduce the use of tobacco and alcohol products to a minimum throughout the study and to refrain from using tobacco or alcohol during study visits
10. Body weight ranging from 45-110 kg (99-242 lbs.) and a body mass index (BMI) of 18-32 kg /m^2 inclusive
11. Prior or Concomitant therapy must be Either monotherapy treatment with levodopa of maximum 600 mg levodopa immediate release or 800 mg levodopa controlled or 1000 mg levodopa dual release, given for at least 90 days, with stable doses for at least 30 days prior to the first dose OR treatment naïve

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
40 years

Upper age limit
85 years

Sex
All

Total final enrolment
61

Key exclusion criteria
Current exclusion criteria as of 24/07/2023:

1. Medical history indicating a Parkinsonian syndrome other than idiopathic PD
2. CNS or psychiatric disorders other than idiopathic PD (mild depression or anxiety arising in the context of PD is not exclusionary)
3. History of brain surgery for PD
4. Use of any of symptomatic drug for PD other than levodopa pramipexole, ropinirole, or

rotigotine within 60 days prior to the first dose
5. Known carriers for mutations in the following genes: alpha-synuclein, LRRK2, GBA, PRKN, PINK1, or DJ1
6. Unstable or clinically significant cardiovascular disease within the last year prior to screening
7. Uncontrolled hypertension
8. Use of oral anticoagulants, low-molecular-weight heparin, warfarin (Coumadin), acenocoumarol, and phenprocoumon is not allowed within 10 days before the first Lumbar Puncture and during the study (low dose aspirin is permitted as monotherapy)
9. Concomitant disease or unstable medical condition within 6 months of screening that could interfere with the study or treatment that might interfere with the conduct of the study, including but not limited to autoimmune disease, immunodeficiency diseases, any active infectious disease
10. History of immunodeficiency diseases
11. Presence of hepatitis B surface antigen (HBsAg) or positive for total hepatitis B core antibody (HBcAb), or positive hepatitis C (HCV) at screening
12. Vaccine(s) other than SARS-CoV2 vaccine within 28 days prior to the first dose, or plans to receive vaccines during the study or within 28 days of the last dose
13. History of chronic liver disease
14. Clinically significant abnormalities in laboratory test results at screening, including hepatic and renal panels, complete blood count, chemistry panel and urinalysis
15. Any previous administration of selnoflast or other compound targeting NLRP3
16. Enrollment in another investigational study
17. Use of any of other investigational therapy (other than protocol-mandated study treatment) within 90 days or 5 drug elimination half-lives (whichever is longer) prior to the first dose

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Previous exclusion criteria:

1. Medical history indicating a Parkinsonian syndrome other than idiopathic PD, including but not limited to progressive supranuclear palsy, multiple system atrophy, drug induced Parkinsonism, essential tremor, vascular Parkinsonism, primary dystonia
2. History of brain surgery for PD
3. Known carriers for mutations in the following genes: α-synuclein, LRRK2, GBA, PRKN, PINK1, or DJ1
4. Diagnosis of dementia or another significant central nervous system (CNS) disease other than PD
5. History of clinically significant abnormality in a Magnetic Resonance Imaging (MRI) scan, including but not limited to prior haemorrhage or infarct
6. Presence of any psychiatric condition (e.g., major depression, schizophrenia, delusion, delirium) at screening or baseline
7. Acute suicidality, as evidenced by answering “yes” for Question 3 or 4 on the C-SSRS scale
8. History of suicidal behaviour such that a determination of “yes” is made on the Suicidal Behaviour section of the C-SSRS for “Actual Attempt”, “Interrupted Attempt”, “Aborted Attempt”, or “Preparatory Acts or Behaviour
9. History of malignancy prior to screening, except for appropriately treated, nonmelanoma skin carcinoma, non-metastatic prostate cancer, treated carcinoma in situ of the cervix or Stage I uterine cancer
10. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of drugs, or which may jeopardize the participant in case of participation in the study
11. History of major vascular surgery within 6 months prior to screening

12. History of clinically significant Electrocardiogram (ECG) abnormalities, or ECG abnormalities at screening or baseline (Day 1)
13. Within the last year prior to screening, unstable or clinically significant cardiovascular disease (e.g., myocardial infarction, major vascular surgery)
14. Uncontrolled hypertension
15. Recent (within the last 3 years prior to screening) and/or recurrent history of clinically significant autonomic dysfunction
16. History of clinically significant severe drug allergies, multiple drug allergies, or anaphylaxis due to gelatine (a constituent of the capsule shell)

Date of first enrolment
22/09/2022

Date of final enrolment
06/06/2024

Locations

Countries of recruitment
United Kingdom

England

Netherlands

United States of America

Study participating centre
UMC St Radboud
Netherlands
6525 GA

Study participating centre
Vanderbilt University Medical Center
United States of America
37232

Study participating centre
University of Alabama at Birmingham
United States of America
35294

Study participating centre

Brain Research Center B.V
Netherlands
1081 GN

Study participating centre
Brain Research Center Zwolle
Netherlands
8025AZ

Study participating centre
Weill Cornell Medical College
United States of America
10065

Study participating centre
NeuroStudies.net, LLC
United States of America
30033

Study participating centre
University Pennsylvania Hospital
United States of America
19104

Study participating centre
Georgetown University
United States of America
20007

Study participating centre
Columbia University
United States of America
10032-3725

Study participating centre
Queen Mary University of London
327

Mile End Road
London
United Kingdom
E1 4NS

Study participating centre
Campus for Ageing & Vitality
Newcastle General Hospital
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NE4 6BE

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St. Georges Hospital
Cranmer Terrace
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United Kingdom
SW17 0RE

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
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W6 8RF

Study participating centre
National Hospital for Neurology & Neurosurgery
Queen Square
London
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WC1N 3BG

Study participating centre
University of Exeter
Stocker Road
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United Kingdom
EX4 4PY

Study participating centre
Cedars Sinai Medical Center
United States of America
90048

Sponsor information

Organisation
Roche (Switzerland)

ROR
https://ror.org/00by1q217

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

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

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes