ForPatients
by Roche

Alzheimer's Disease (AD)

A study to see the effects of different doses of nivegacetor (RO7269162) in people with or without an inherited gene that causes Alzheimer's disease

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	BP44161 ISRCTN75434529

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:

A single-center, Adaptive, Repeated Dose Phase I Study to Investigate the Pharmacodynamics of RO7269162 Following Oral Administration in Presymptomatic PSEN1 E280A Mutation Carriers and in Non-Carriers from the Same Kindred in Autosomal-Dominant Alzheimer's Disease

Trial Summary:

The purpose of this phase is to see how safe the treatment is, and how different doses may change biological markers of Alzheimer's disease in individuals that may carry a change in the Presenilin 1 gene.

F. Hoffmann-La Roche Ltd	Phase 1
Sponsor	Phase

BP44161 ISRCTN75434529
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	18 to 25 years	Yes

1. Why was this study needed?

Alzheimer's disease is a medical condition caused by changes in the brain. It affects memory, thinking and behaviour, usually starting slowly and getting worse over time until it interferes with daily life.

One of the main causes of Alzheimer's disease is the build-up of a substance in the brain called beta-amyloid. These plaques form more easily when there are “long” forms of beta-amyloid (especially one called ‘Abeta42’). Shorter forms of beta-amyloid (such as Abeta37 and Abeta38) do not form beta-amyloid plaques.

Some people have a change (mutation) in a gene called Presenilin1. These people - called ‘carriers’ - make extra amounts of the long form Abeta42 and can cause the carriers to develop Alzheimer's disease before the age of 60. People without this change in the gene - called ‘non-carriers’ - can also develop Alzheimer's disease for other reasons, but if so usually later in life.

This study is testing a medicine called nivegacetor designed to slow or stop the build-up of beta-amyloid plaques by shifting production toward the shorter forms. This may delay or prevent Alzheimer's disease. Researchers did this study to assess how multiple doses of nivegacetor affect biological markers of Alzheimer’s disease in the blood and spinal fluid (specifically Abeta42 levels) in carriers and non-carriers of the changed Presenilin1 gene. Researchers also wanted to find out if nivegacetor was safe.

2. How was the study conducted?

This study invited members of a large family in Colombia that is known to include some members that carry a change in the Presenilin1 gene. Each participant gave a blood sample to test whether or not they were ‘carriers’ of the gene change. Neither the participants nor the study doctors were told the test results. This was done at the request of the family, so that no one would find out their genetic status as part of the study. Both carriers and non-carriers were able to take part in the study.

Participants were randomly placed into 3 groups and given either a low, medium or high dose of nivegacetor as capsules once daily for 7 days. During the study, samples of blood and the fluid that surrounds the brain and spinal cord (called cerebrospinal fluid, or CSF) were collected.

3. What were the results of the study?

The highest dose reduced the long forms of beta-amyloid the most, in both blood and brain fluid, and worked similarly in people with and without the change in the Presenilin1 gene

Nivegacetor was generally well tolerated at all dose levels tested. Unwanted effects were manageable and there were no serious unwanted effects.

Inclusion Criteria:

- 18 to 25 years of age inclusive

- Membership in gene mutation carrier kindred. Gene mutation carrier or non-carrier status will have been confirmed prior to or during the screening period
- Body mass index (BMI) of 18-32 kilograms per metre square (kg/m^2) inclusive

Exclusion Criteria:

- Any clinically relevant finding, condition or disease detected during the medical interview/physical examination at screening or Day -1.
- History or evidence of any medical condition capable of significantly altering the absorption, metabolism, or elimination of drugs, including surgical history affecting gastric motility or altering the gastrointestinal tract.
- History of convulsions
- Participants who, in the investigator`s judgment, pose a suicidal or homicidal risk
- Vaccination within 6 weeks prior to Day 1 including influenza and/or SARS-CoV-2/COVID-19 vaccination.
- Positive result on human immunodeficiency virus 1 (HIV1) and HIV2, hepatitis C virus (HCV) or hepatitis B (HBV).
- Participants who test positive for acute respiratory syndrome coronavirus 2 (SARSCoV-2) on admission to the study site