Long-term extension safety and efficacy study of SAR442168 in participants with relapsing multiple sclerosis.

Published: 15-04-2019
Last updated: 17-01-2025

Primary: to determine the long-term safety and tolerability of SAR442168 in RMS participants. Secondary: to evaluate efficacy of SAR442168 on disease activity, assessed by clinical and imaging methods.

Ethical review	Approved WMO
Status	Completed
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON54729

Source
ToetsingOnline

Brief title
LTS16004

Condition

- Demyelinating disorders

Synonym
demyelinating disease, Multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi B.V.
Source(s) of monetary or material Support: Genzyme Europe

Intervention

Keyword: autoimmune disease, Bruton's tyrosin kinase inhibitor, Multiple sclerosis, RMS

Outcome measures

Primary outcome

Adverse events (AEs), serious adverse events (SAEs), safety findings on magnetic resonance imaging (MRI), potentially clinically significant abnormalities (PCSAs) in laboratory tests, electrocardiogram (ECG), or vital signs during the study period.

Secondary outcome

- Number of new gadolinium (Gd)-enhancing T1-hyperintense lesions by brain MRI
- Number of new or enlarging T2 lesions
- Total number of Gd-enhancing T1-hyperintense lesions
- Number of relapses (annualized relapse rate [ARR]) during the study period
- Change in Expanded Disability Status Scale (EDSS) score from baseline over time

Study description

Background summary

The Bruton's tyrosine kinase (BTK) pathway is critical to signaling in B lymphocytes and myeloid cells including central nervous system (CNS) microglia. Each of these cell types has been implicated in the pathophysiology of multiple sclerosis (MS). Accordingly, SAR442168, a CNS-penetrant BTK inhibitor has the potential for a dual mechanism of action by inhibiting antigen-induced B-cell activation responsible for inflammation and by modulating maladaptive microglial cells linked to neuroinflammation in the brain and spinal cord. There is still a significant unmet need for therapies that target neuroinflammation in the CNS with a goal of halting long term disability and neurodegeneration in people with relapsing multiple sclerosis (RMS), and also

in progressive forms of the disease (primary progressive multiple sclerosis [PPMS] and secondary progressive multiple sclerosis SPMS]). Even the most recent high-efficacy disease-modifying therapies act mainly on adaptive immunity in the periphery with only modest or temporary ability to halt neuroinflammatory and neurodegenerative processes and stop disease progression, as also demonstrated by recent studies in progressive MS.

Study objective

Primary: to determine the long-term safety and tolerability of SAR442168 in RMS participants.

Secondary: to evaluate efficacy of SAR442168 on disease activity, assessed by clinical and imaging methods.

Study design

A long-term, phase 2, Single Group Treatment study for participants previously treated in the DRI15928 study. It consists of 2 parts: Part A, which is blinded for participants and Investigators during the double-blind period of the study, and Part B which is an open-label period of the study.

Intervention

Bruton's tyrosine kinase inhibitor. In phase A of the study the patient receives a maximum of four tablets per day to achieve a daily dose of 5, 15, 30 or 60 mg, depending on the arm to which the patient was randomized in the previous DRI15928 study. This is given in tablet form and the route of administration is oral. In phase B of the study the patient will be transferred to the optimal dose of SAR442168, 60mg, as determined from the DRI15928, and the study will be open-label.

Study burden and risks

Risks and burdens related to blood collection, study procedures and possible adverse events of study medication.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Participants must have completed treatment in the DRI15928 study
- Female participants must continue to use an acceptable effective contraception method of birth control from inclusion and until the last study dose, except if she has undergone sterilization at least 3 months earlier or is postmenopausal.

Exclusion criteria

-The participant has a confirmed concomitant laboratory or ECG abnormality or medical condition
deemed by the investigator incompatible with continuation of SAR442168 treatment.
-The participant has received any live (attenuated) vaccine (including but not limited to varicella
zoster, oral polio, and nasal influenza) between the last DRI15928 visit and the first treatment visit
in the LTS16004 study.
-The participant has received a non-study MS disease modifying treatment between the last IMP
treatment in Study DRI15928 and inclusion in Study LTS16004, which by judgement

of the
Investigator may add unjustified risk to switching back and continuing
trreatment with SAR442168.
Washout periods after treatment with non-study DMTs should be respected except for interferons or
glatiramer acetate treatment.
-The participant is receiving strong inducers or inhibitors of CYP3A or CYP2C8 hepatic enzymes.
Note: Such drugs need to be stopped at least 5 half-lives before study drug administration.
The participant is receiving anticoagulant/antiplatelet therapies, including:
• Acetylsalicylic acid (aspirin)
• Antiplatelet drugs (eg, clopidogrel)
• Warfarin (vitamin K antagonist)
• Heparin, including low molecular weight heparin (antithrombin agents)
• Dabigatran (direct thrombin inhibitor)
• Apixaban, edoxaban, rivaroxaban (direct factor Xa inhibitors)
Note: All above drugs need to be stopped at least 5 half-lives before study drug administration
except for aspirin, which needs to be stopped at least 8 days beforehand.
-Prior/concurrent clinical study experience
-The participant is taking part in another interventional clinical trial of another drug substance.
-Uncooperative behavior or any condition that could make the participant potentially non-adherent
with the study procedures

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Completed

Start date (anticipated):	04-12-2019
Enrollment:	1
Type:	Actual

Ethics review

Approved WMO Date:	15-04-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-08-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-004731-76-NL
CCMO	NL68933.029.19
Other	U1111-1223-4256