A randomized, double-blind, placebo-controlled single and multiple ascending dose study of the safety, tolerability and pharmacokinetics of oral doses of SAR443122 in healthy adult subjects.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON48479

Source
ToetsingOnline

Brief title
SAD and MAD of SAR443122

Condition

- Autoimmune disorders

Synonym
Auto immune disease

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: Immune system disease, RA, SAR443122

Outcome measures

Primary outcome

To assess the tolerability and safety of SAR443122 after single ascending oral doses in healthy adult subjects.

To explore relative bioavailability between study formulation (SF) and solid dosage form (SDF) formulation of SAR443122

To explore the effect of a high-fat meal on the PK of the SDF formulation of SAR443122

To assess the tolerability and safety of 14-day ascending repeated oral doses of SAR443122 in healthy adult subjects

Secondary outcome

To determine the pharmacokinetic (PK) parameters of SAR443122 after single ascending oral doses in healthy adult subjects

To determine the pharmacokinetic parameters of SAR443122 after ascending repeated oral doses in healthy adult subjects

Study description

Background summary

SAR443122 is a new compound that may eventually be used for the treatment of autoimmune diseases such as rheumatoid arthritis, an inflammatory disease. In autoimmune diseases, the immune system sees the body's own cells and substances as foreign and attacks them.

Rheumatoid arthritis is a long-lasting autoimmune disorder that primarily affects the joints. Inflammation is characterized by increased blood supply and activation of defense mechanisms, resulting in redness, swelling, heat and pain.

The study compound that will be researched in this study, SAR443122, inhibits a protein (RIPK1) that is involved in abnormal immune function seen in inflammatory diseases.

Study objective

This study will be performed in a maximum of 97 healthy volunteers. The study will be performed in 2 parts, Part 1 (split up in Part 1a and Part 1b) and Part 2. A single dose of SAR443122 (or placebo [only in Part 1a]) will be administered in Part 1 whereas multiple doses of SAR443122 (or placebo) will be administered in Part 2.

The purpose of this study is to investigate how safe the new compound SAR443122 is and how well it is tolerated when it is administered to healthy volunteers. It will also be investigated how quickly and to what extent SAR443122 is absorbed (taken up), distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). Further, the pharmacokinetics of SAR443122 when it is administered as 2 different manufactured oral capsules (Part 1b only). This comparison of pharmacokinetics is called relative bioavailability. In addition, the effect of food on the absorption of SAR443122 in the body will be investigated (Part 1b only). Also, the effect of SAR443122 on certain signaling proteins in your body will be investigated (this is called pharmacodynamics).

SAR443122 will be tested at various dose levels. The effects of SAR443122 will be compared to the effects of a placebo (not in Part 1b). A placebo is a capsule that does not contain any active medicine. Whether you will receive SAR443122 or placebo will be determined by chance. Please note that when the term *study compound* is used in this document, this can refer to SAR443122, placebo, or both.

SAR443122 has not been administered to humans before. It has been previously tested in the laboratory and on animals.

Study design

Part 1a
A single dose of the study agent (SAR443122 or placebo) will be given as capsules by mouth with 240 milliliters (mL) of water. No chewing is allowed on the capsules. The test substance will be administered after fasting for at least 10 hours (fasting: no food or drink except water). After administration of the test substance, volunteers will fast for a period of 4 hours until the planned lunch. They may drink water during fasting, except from the time of administration of the test substance until 1 hour thereafter. The actual research will consist of 1 period during which the volunteers will stay in the research center for 5 days (4 nights). The research center is expected at 2 p.m. in the afternoon on Day -1, the day before Day 1 (Day 1 is the day on which the study drug is administered). They leave the research center on Day 4.

Part 1b
A single dose of SAR443122 is given in each of 3 periods: once as capsules by mouth after fasting (fasting: no food and drink except water), once as capsules (but with a different composition) by mouth after fasting and once as capsules by mouth after having received a high-fat breakfast. The order in which one receives these treatments is determined by drawing lots. There will be a period of at least 7 days between each administration of the study compound. Each period, SAR443122 is given as oral capsules with 240 milliliters (ml) of water. No chewing is allowed on the capsules. The actual research will consist of 3 periods in which the volunteers will stay in the research center for 5 days (4 nights) in each period. Each volunteer is expected in the research center at 2:00 p.m. on Day -1, the day prior to Day 1 (Day 1 is the day on which SAR443122 is administered). They leave the research center on Day 4 of each period.

Part 2
The actual research will consist of 1 period during which the volunteers will stay in the research center for 18 days (17 nights). They are expected in the research center at 2:00 p.m. on Day -1, the day prior to Day 1 (Day 1 is the day the study drug is administered). They leave the research center on Day 17.

Intervention

Group 1a:
Group 1 day 1; SAR443122 10 milligrams (mg) or placebo; once fasted
Group 2 day 1; SAR443122 30 mg or placebo; once fasted
Group 3 day 1; SAR443122 100 mg or placebo; once fasted
Group 4 day 1; SAR443122 200 mg or placebo; once fasted

Group 5 day 1; SAR443122 400 mg or placebo; once fasted
Group 6 day 1; SAR443122 X mg or placebo; once fasted

Group 1b:
9 volunteers
Period 1 Once 100 milligrams (mg) of SAR443122 as capsules by mouth under fasting conditions
Period 2: Once 100 mg of SAR443122 as capsules by mouth under fasting conditions
Period 3: Once 100 mg SAR443122 as capsules by mouth after a high-fat breakfast

Group 2
Group 8: Day 1-14; SAR443122 W mg or placebo; once a day fasted
Group 9: Day 1-14; SAR443122 X mg or placebo; once a day fasted
Group 10: Day 1-14; SAR443122 Y mg or placebo; once a day fasted
Group 11: Day 1-14; SAR443122 Z mg or placebo; once a day fasted

Study burden and risks

As SAR443122 will be administered to man for the first time in this study, side effects of SAR443122 in man have not been reported to date. However, SAR443122 has been studied extensively in the laboratory and in animals. SAR443122 was safe and well tolerated in animals. At very high repeated doses in 1 animal, a potential effect on the immune system was seen, such as increased white blood cell counts, anemia, increased spleen weight and increased cellularity (formation of blood cellular components) in the bone marrow. You will be monitored for effects on your immune system throughout the study. Except for this finding, based on the animal research and knowledge about the mechanism of action of SAR443122, no specific or pronounced side effects are expected at the moment.

Drawing blood and/or insertion of the indwelling cannula (thin tube in an arm vein) may be painful or cause some bruising.

Contacts

Public
Sanofi-aventis

Avenue Pierre Brossolette 1
Chilly Mazarin Cedex 91385
FR
Scientific
Sanofi-aventis

Avenue Pierre Brossolette 1
Chilly Mazarin Cedex 91385
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy male or female subjects
18 - 55 years
50 - 100 kg
BMI 18.0 - 30.0 kg/m2

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-06-2019
Enrollment:	97
Type:	Actual

Ethics review

Approved WMO Date:	17-06-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-06-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2019-001350-25-NL
CCMO	NL70334.056.19