A randomized, double-blind, placebo-controlled study of the tolerability, pharmacokinetics and pharmacodynamics of ascending single and repeated subcutaneous doses of SAR444336 in healthy adult participants

Published: 01-09-2021
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Primary objective- To assess the tolerability and safety of SAR444336 after single and repeated ascending subcutaneous doses Secondary objectives- To assess the PK parameters of SAR444336 after single ascending subcutaneous doses (Part 1)- To assess...

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

Summary

ID

NL-OMON54131

Source
ToetsingOnline

Brief title
Safety, PK and PD of SAD and MAD of SAR444336 in HV

Condition

- Autoimmune disorders

Synonym
autoimmune disorders, inflammatory disorders

Research involving

Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: FIH, MAD, SAD

Outcome measures

Primary outcome

Number of subjects with treatment-emergent adverse events (TEAEs)

Clinical laboratory evaluations including eosinophils, procalcitonin, and

c-reactive protein (CRP)

Vital signs

12-lead electrocardiogram (ECG)

Secondary outcome

Plasma PK parameters: Cmax, tmax, AUClast, AUC, t1/2z, CL/F

Anti-SAR444336 antibodies

Study description

Background summary

This phase 1 study will assess the safety and tolerability, and characterize the pharmacokinetic (PK) and pharmacodynamic (PD) profile of SAR444336 in healthy subjects following single- and repeated-dose administrations as a first step in clinical development prior to administering this new investigational medicinal product (IMP) to patients.

Study objective

Primary objective

- To assess the tolerability and safety of SAR444336 after single and repeated ascending subcutaneous doses

Secondary objectives
- To assess the PK parameters of SAR444336 after single ascending subcutaneous doses (Part 1)
- To assess the PK parameters of SAR444336 after repeated ascending subcutaneous doses (Part 2)
- To assess anti-drug antibody (ADA) incidence after single and multiple dosing

Exploratory objectives
- To assess the immunophenotyping PD parameters in peripheral blood after single and repeated ascending subcutaneous doses of SAR444336
- To obtain PD parameters after KLH challenge and repeat doses of SAR444336 (Part 2 only)
- To assess the epigenetics of Tregs
- To assess cytokines secretion in plasma
- To collect DNA samples
- To explore the functionality of Treg cells in vitro

Study design

Phase 1, multiple-center, first-in-human (FIH) study in 2 parts combined under one study protocol:
• Part 1, SAD; double-blind (sponsor-unblinded), randomized, placebo-controlled, sequential ascending single doses.
• Part 2, MAD; double-blind (sponsor-unblinded), randomized, placebo-controlled, sequential ascending repeated doses

Intervention

Subcutaneous injections of SAR444336 or placebo (Part 1 single dose, part 2, multiple dose for up to 28 days)
Subjects of part B will receive KLH as challenge drug

Study burden and risks

No benefit is expected for healthy volunteers participating in this study. Considering the measures taken to minimize risk to participants enrolled in this study, there is no unreasonable and significant risk of illness or injury for the participants. In this FIH study, healthy participants between 18 and 55 years of age will be included (both men and women in Part 1, men only in Part 2). Specific criteria for inclusion of study participants considering the mechanism of action of SAR444336 and potential risk associated with treatment, but also study-specific procedures, will be applied.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Part 1
- Male and female participants between 18 and 55 years of age inclusive.
- Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and ECG.
- Laboratory values within normal range unless the abnormality is considered not clinical relevant by the investigator.
- Eosinophils <500 cells/µL
- Normal vital signs after 10 minutes resting in supine position
- Standard 12-lead ECG parameters after 10 minutes resting in supine position in the normal ranges and normal ECG tracing unless the Investigator considers an ECG tracing abnormality to be not clinically relevant.
- Body weight between 50 - 110 kg (inclusive) and body mass index (BMI) between 18 - 30*kg/m2 (inclusive) at screening.

Part 2
- Male participants between 18 and 55 years of age inclusive.
- Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and ECG.
- Laboratory values within normal range unless the abnormality is considered not clinical relevant by the investigator.
- Eosinophils <500 cells/µL
- Normal vital signs after 10 minutes resting in supine position
- Standard 12-lead ECG parameters after 10 minutes resting in supine position in the normal ranges and normal ECG tracing unless the Investigator considers an ECG tracing abnormality to be not clinically relevant.
- Body weight between 50 - 110 kg (inclusive) and body mass index (BMI) between 18 - 30*kg/m2 (inclusive) at screening.
- Fitzpatrick skin type I - III

Exclusion criteria

Part 1
- Any disease associated with immune system dysfunction.
- Known polyethylene glycol allergy
- Any current active viral, bacterial or fungal infection or any medically relevant infection having occurred within 3 weeks before inclusion.
- Any history or presence of clinically relevant cardiovascular, pulmonary, gastrointestinal, hepatic, renal, metabolic, hematological, neurological, osteomuscular, articular, psychiatric, autoimmune, systemic, ocular, or infectious disease, or signs of acute illness that would pose an unacceptable risk to the subject in the opinion of the investigator.
- Frequent headaches and/or migraine, recurrent nausea and/or vomiting (for vomiting only, more than twice a month).
- Blood donation >500 mL within 2 months before inclusion.
- Symptomatic postural hypotension, irrespective of the decrease in blood pressure, or asymptomatic postural hypotension defined as a decrease in systolic blood pressure >=30*mmHg within 3 minutes when changing from supine to standing position.
- Presence or history of drug hypersensitivity, or allergic disease diagnosed and treated by a physician, except for history of mild allergic diseases which are not active at the time of inclusion and considered not clinically relevant in the opinion of the investigator.
- History or presence of drug or alcohol abuse.
- Smoking regularly more than 10 cigarettes or equivalent per week, unable to stop smoking during the study (occasional smoker can be enrolled).
- Excessive consumption of beverages containing xanthine bases.
- Presence or history of any atopic disease.
- Non-live vaccines including: last administration of a vaccine within 4 weeks before randomization; non-live COVID-19 (booster) vaccination within 14 days

before randomization. First (and second, if applicable) COVID-19 vaccinations are not allowed within 4 weeks before randomization.
- Live vaccines: Last administration of a vaccine within 3 months before randomization.
- Immunomodulatory medication within 60 days before screening.
- Any medication (including St John*s Wort) within 14 days before inclusion or within 5*times the elimination half-life or pharmacodynamic half-life of the medication; any vaccination within the last 28 days (except COVID-19 booster vaccination) and any biologics (antibody or its derivatives) given within 4 months before inclusion.
- Positive result on any of the following tests: hepatitis B surface (HBs Ag) antigen, antihepatitis B core antibodies (anti-HBc Ab), anti-hepatitis C virus (anti-HCV) antibodies, anti-HIV1 and anti HIV2 Ab.
- Positive result on urine drug screen.
- Positive alcohol breath or urine test.

Part 2
- Participants are excluded from the study if any of the following criteria apply:
- Any disease associated with immune system dysfunction.
- Known seafood allergy
- Known polyethylene glycol allergy
- Any current active viral, bacterial or fungal infection or any medically relevant infection having occurred within 3 weeks before inclusion.
- Any history or presence of clinically relevant cardiovascular, pulmonary, gastrointestinal, hepatic, renal, metabolic, hematological, neurological, osteomuscular, articular, psychiatric, autoimmune, systemic, ocular, or infectious disease, or signs of acute illness that would pose an unacceptable risk to the subject in the opinion of the investigator.
- Frequent headaches and/or migraine, recurrent nausea and/or vomiting (for vomiting only, more than twice a month).
- Blood donation >500 mL within 2 months before inclusion.
- Symptomatic postural hypotension, irrespective of the decrease in blood pressure, or asymptomatic postural hypotension defined as a decrease in systolic blood pressure >=30*mmHg within 3 minutes when changing from supine to standing position.
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before randomization. First (and second, if applicable) COVID-19 vaccinations are not allowed within 4 weeks before randomization.
- Live vaccines: Last administration of a vaccine within 3 months before randomization.
- Immunomodulatory medication within 60 days before screening.
- Participants with known previous exposure to KLH.
- Any medication (including St John*s Wort) within 14 days before inclusion or within 5 times the elimination half-life or pharmacodynamic half-life of the medication; any vaccination within the last 28 days (except COVID-19 booster vaccination) and any biologics (antibody or its derivatives) given within 4 months before inclusion.
- Positive result on any of the following tests: hepatitis B surface (HBs Ag) antigen, antihepatitis B core antibodies (anti-HBc Ab), anti-hepatitis C virus (anti-HCV) antibodies, anti-HIV1 and anti HIV2 Ab.
- Positive result on urine drug screen.
- Positive alcohol breath or urine test

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):	15-10-2021
Enrollment:	104
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SAR444336

Generic name:	NA

Ethics review

Approved WMO Date:	01-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-10-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-12-2022
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2023
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	EUCTR2021-003021-30-NL
ClinicalTrials.gov	NCT05876767
CCMO	NL78466.056.21