A randomized, double-blind, placebo-controlled, first-in-human phase 1 study evaluating safety, tolerability, and pharmacokinetics of single ascending doses of SOL-116 (a humanized monoclonal anti-BSSL antibody) in healthy subjects and patients with rheumatoid arthritis.

Published: 19-09-2022
Last updated: 27-12-2024

Single dosingPrimary objective:• To evaluate the safety and tolerability of single ascending doses of SOL-116 in healthy subjects and rheumatoid arthritis (RA) patients.Secondary objective:• To determine single dose pharmacokinetic (PK)…

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

Summary

ID

NL-OMON56208

Source
ToetsingOnline

Brief title
CS0382-210463

Condition

- Autoimmune disorders

Synonym
rheumatoid arthritis (RA)

Research involving
Human

Sponsors and support

Primary sponsor: Lipum AB
Source(s) of monetary or material Support: Lipum AB

Intervention

Keyword: pharmacokinetics, safety, tolerability

Outcome measures

Primary outcome

Adverse events (type, frequency, severity, and relationship of adverse events (AEs) to study drug treatment), clinical laboratory evaluations (including blood haematology/plasma biochemistry analyses and urinalyses), immune reactions, vital signs, electrocardiogram (ECG) and injection site reactions.

Secondary outcome

All parts

• PK of SOL-116 variables: area under the serum concentration-time from time zero to infinity (AUC0-inf), AUC from time zero to time t of the last measured concentration above the limit of quantification (AUC0-t), maximum observed serum concentration (Cmax), time to Cmax (Tmax), terminal elimination half-life (T1/2), apparent volume of distribution (Vz/F), apparent total body clearance (CL/F) and dose proportionality after single dose (based on AUC and Cmax).

• Incidence and titre of anti-drug antibodies (ADA) to SOL-116.

Multiple dosing

• PK of SOL-116 variables for the last dose: area under the serum

concentration-time from time zero to the end of dosing interval (AUC0-tau),

maximum observed serum concentration (Cmax), time to Cmax (Tmax), minimum

observed serum concentration (Ctrough), average serum concentration (Cave),

apparent total body clearance at steady state (CLss/F), time to steady state,

accumulation ratio in Cmax and AUC0-tau

Study description

Background summary

RA is a chronic autoimmune inflammatory joint disease characterized by a varying number of swollen, stiff and painful joints typically in hands and feet, but any joint may be affected. With time, erosion of joints and bone results in varying degree of disability and loss of quality of life.
The treatment of RA is still associated with high unmet medical need (4). Synthetic disease-modifying antirheumatic drugs (sDMARDs) and steroids, which are key in initial treatment of RA, are all associated with adverse effects (AE) and thus intolerability (e.g., gastrointestinal, pulmonary, infectious and hematologic AEs.
Given the preclinical data at hand (see below) and the new mechanism of action targeting an alternative inflammatory pathway compared to the approved products, it is believed that SOL-116 may demonstrate significant benefit in patients not responding satisfactory, or responding transiently, to current therapies, as well as those who suffer from serious adverse effects. The candidate drug SOL-116 may be used as a standalone treatment, or in combination with other treatments, including sDMARDs but also other bDMARDs to reduce the risk of lost efficacy.

Study objective

Single dosing
Primary objective:
• To evaluate the safety and tolerability of single ascending doses of SOL-116 in healthy subjects and rheumatoid arthritis (RA) patients.
Secondary objective:
• To determine single dose pharmacokinetic (PK) characteristics of SOL-116 in

healthy subjects and RA patients.
• To assess the immunogenicity of SOL-116 after single SC doses in healthy subjects and RA patients.

Multiple dosing
Primary objective:
• To evaluate the safety and tolerability of multiple dosing of SOL-116 in healthy subjects.
Secondary objective:
• To determine multiple dose PK characteristics of SOL-116 in healthy subjects.
• To assess the immunogenicity of SOL-116 after multiple SC doses in healthy subjects.

Study design

This is a randomised, double-blind, placebo-controlled phase 1, first-in-human (FIH) study designed to evaluate the safety, tolerability and pharmacokinetics (PK) of single subcutanous ascending doses of SOL-116 in healthy subjects and adult patients with RA.

Intervention

SOL-116 (100 mg/mL) - subcutaneous administration or Matching placebo (saline or vehicle) - subcutaneous administration

Study burden and risks

SOL-116 plasma concentrations in the planned single ascending dose (first in human) study are predicted to be well below the levels where adverse effects may start to develop. Patients participating in clinical trials must be closely monitored for any adverse events, and laboratory, physical examination, ECG, or vital signs abnormalities. As with all investigational compounds, the potential exists for unanticipated serious or life threatening toxicities or adverse events not predicted by the animal toxicology conducted to date. Investigators should exercise vigilance in the monitoring of patients involved in this clinical trial with SOL-116. The combined safety data from the pre-clinical studies have not revealed any safety issues that would outweigh the expected benefits. The planned study assessments are considered sufficient to meet the scientific and medical goals for the study. Given the high medical need of additional therapy with a novel mechanism of action it is therefore concluded that the potential benefits from assessment of the scientific objectives in the study outweigh the potential risks for the treated subjects.

Contacts

Public
Lipum AB

Tvistevägen 48C
Umeå SE-907 36
SE
Scientific
Lipum AB

Tvistevägen 48C
Umeå SE-907 36
SE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Willing and able to give written informed consent for participation in the study and is willing and able to abide by the study restrictions.
2. Males and females aged between 18 and 65 years (inclusive) at Screening. For patients in the RA cohort, an age interval between 18 and 70 years (inclusive).
3. Normal clinically physical findings, apart from RA specific findings (including deviating laboratory values e.g., mild anaemia or swollen joints) for RA patients, including pulse rate, blood pressure, electrocardiogram (ECG), physical examination, and laboratory values (haematological/clinical chemistry) as judged by the Investigator. Healthy subjects must be negative for anti-CCP and have Rheumatoid Factor <1.5 ULN at Screening.
4. For Parts 1 and 3, body mass index (BMI) between 19.0 and 30.0 kg/m2 and body weight between 50 to 100 kg (inclusive) at Screening. For Part 2, body

weight between 50 to 120 kg (inclusive) at Screening.
5. Sexually active male patients participating in the study must use a barrier method of contraception (condom) and refrain from sperm donation during the study and for at least 150 days after last dosing if their female sexual partner is of childbearing potential. Acceptable methods of birth control for female partners of male subjects are: hormonal contraceptives (oral contraceptives, implant or injection), intrauterine device (placed at least 1 month before the start of the study). Surgical sterilization of male patients can be accepted as a form of birth control if the sterilization procedure took place at least 6 months prior to the start of the study.
6. Females of childbearing potential must during the study and for at least 230 days after last dosing utilise a method of contraception that can achieve a failure rate of less than 1% per year when used consistently and correctly. Such highly effective birth control methods include:
• combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
o oral
o intravaginal
o transdermal
• progestogen-only hormonal contraception associated with inhibition of ovulation:
o oral
o injectable
o implantable
• intrauterine device (IUD)
• intrauterine hormone-releasing system (IUS)
• bilateral tubal occlusion
• vasectomized partner
• sexual abstinence
7. Females of non-childbearing potential must fulfil one of the following:
• Irreversibly surgically sterile i.e., hysterectomy, bilateral salpingectomy, the fallopian tubes have been blocked or sealed (sterilization), and bilateral oophorectomy.
• Spontaneous amenorrhoea during the last 12 months prior to enrolment, and having follicle stimulating hormone (FSH) levels in the postmenopausal range (i.e. >= 30 mIU/mL) at Screening.
The following inclusion criterion is only applicable for RA patients:
8.Fulfilling the 2010 American College of Rheumatology (ACR)/European Union League Against Rheumatism (EULAR) classification criteria for RA [8].
• Treatment with MTX for at least 12 weeks prior to treatment start and planned to continue with MTX during the study; if the MTX dose was changed during the 12-week period, such a patient may be included in the study based on Investigator judgement.
• Patients naïve to biological disease modifying anti-rheumatic drug (bDMARD) or who are washed out (at least 5 half-lives) from such therapy before study drug dosing.
• Patients naïve to conventional/targeted synthetic disease modifying

anti-rheumatic drug (csDMARD/tsDMARD), except for MTX, or who are washed out since at least 12 weeks from such therapy before study drug dosing.
• Use of oral glucocorticosteroids is allowed if equivalent to <=5 mg/day of prednisolone on a stable dose for a least 4 weeks prior to dosing (Day 1) and expected to remain on that dose level for at least 4 weeks after dosing (Day 1).

Exclusion criteria

1. History of any clinically significant acute inflammatory joint disease (for the RA cohort; other than RA).
2. Any chronic or long-lasting disease which may interfere with the study objectives or jeopardise the safety of the subjects/patients as judged by the Investigator or responsible physician (for the RA cohort; other than RA).
3. Ongoing infection on Day-1.
4. Serious infection treated with antibiotics and evaluated by physician in the past 14 days prior to Day -1.
5. Current treatment with heparin products.
6. Use of any prescription or non-prescription drugs (excluding paracetamol, hormonal contraceptives), antacids, herbal, and dietary supplements (including St John*s Wort) within 14 days (or 28 days if the drug is a potential hepatic enzyme inducer) or 5 half-lives (whichever is longer) prior to the first dose of study drug for healthy subjects and within 4 weeks prior to the first dose of study drug for RA patients, unless in the opinion of the Investigator the medication will not interfere with the study procedures or compromise subject/patient safety. In RA patients, MTX and folic acid use are exempted.

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:	Completed
Start date (anticipated):	21-10-2022
Enrollment:	72
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.

Ethics review

Approved WMO Date:	19-09-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-09-2022
Application type:	First submission
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:	09-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	28-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-08-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2024
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	EUCTR2022-001489-37-NL
CCMO	NL81346.056.22