Phase 2, randomized, parallel-group, double-blind, placebo-controlled study of sonelokimab in patients with active moderate to severe hidradenitis suppurativa

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Primary Objective:1. To evaluate the efficacy of sonelokimab at 2 different dose levels (120 mg, 240 mg) compared with placebo in the treatment of participants withactive moderate to severe hidradenitis suppurativa.Secondary Objectives:1. To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON51658

Source
ToetsingOnline

Brief title
MoonLake M1095-HS-201 (6012/0002)

Condition

- Epidermal and dermal conditions

Synonym
□boil-like□ lumps or abscesses that can occur in the armpits, buttocks or under the breasts., groin, Hidradenitis Suppurativa (acne inversa); It□s characteristics include recurrent, painful nodules, perianal area

Research involving

Human

Sponsors and support

Primary sponsor: -
Source(s) of monetary or material Support: MoonLake Immunotherapeutics AG

Intervention

Keyword: hidradenitis suppurativa (acne inversa), MoonLake M1095-HS-201 (6012/0002), parallel design, Phase 2, Sonelokimab

Outcome measures

Primary outcome

1. Percentage of participants achieving Hidradenitis Suppurativa Clinical

Response (HiSCR) 75 at Week 12, where HiSCR75 is defined as at

least a 75% reduction from baseline in abscess and inflammatory nodule (AN)

count, with no increase from baseline in abscess or draining fistula

count.

Secondary outcome

1. Proportion of participants achieving HiSCR50 at Week 12.

2. Change from baseline in International Hidradenitis Suppurativa Severity

Score System (IHS4) at Week 12;

3. Proportion of participants achieving a Dermatology Life Quality Index (DLQI)

total score of <=5 at Week 12.

4. Proportion of participants achieving at least 30% reduction and at least

1-unit reduction from baseline in Numerical Rating Scale (NRS) 30

in Patient's Global Assessment of Skin Pain (PGA) of Skin Pain at Week 12 among

subjects with baseline NRS >=3.

Study description

Background summary

Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent debilitating skin disease that usually presents in early adulthood. Predisposing risk factors include family history, with ~34% of first-degree relatives affected, in addition to smoking and obesity. HS manifests as painful inflammatory skin lesions in the axillary, inguinal, gluteal, and perianal regions and is characterized by inflammatory nodules and abscesses complicated by the formation of pusdischarging dermal tunnels, also known as sinus tracts or fistulas. Dermal tunnels are a unique morphologic feature of HS, recognized as a source of inflammation and an active mediator of disease pathogenesis. Clinically, tunnels cause significant pain and morbidity for patients, and are predictors of poor prognosis and a more aggressive disease course.

Over time, chronic, uncontrolled, and inadequately treated inflammation results in irreversible tissue destruction and scarring, which is not susceptible to medical therapy. Severe scarring is associated with further debilitating complications, including contractures, limitations in limb mobility, and lymphedema. Once fibrotic architectural changes occur, surgery is the only recommended therapeutic option to reduce the volume of fibrotic tissue and symptom burden; however, recurrence rates following surgery are significant. Therefore, targeting the
inflammatory phase of HS and reducing inflammatory lesion burden should be a core element of disease management to prevent irreversible tissue destruction and debilitation.

The high symptom burden of HS (chronic pain, large amounts of purulent secretions, malodor, and fatigue) has a profound impact on patient quality of life and contributes to a significant deterioration in physical and mental health. People with HS suffer from greater pain and associated psychologic comorbidities, including depression, anxiety, disability, and impairments in quality of life, compared with those with other dermatologic conditions.

Management of HS requires a multifaceted approach, which may include lifestyle modifications, pain management, topical therapies (antibiotics, antiseptics, and intralesional corticosteroids), systemic therapies (antibiotics, retinoids, and biologics), and invasive surgical treatments (incision and drainage of active lesions, deroofing procedures, and radical excision) The only approved biologic treatment option for patients with moderate to severe HS is the anti-tumor necrosis factor (TNF) inhibitor adalimumab (Humira®).

Sonelokimab
Sonelokimab is a tri-specific nanobody that selectively inhibitsIL-17A and

IL-17F. The central moiety binds to serum albumin to extend the half-life in vivo. Sonelokimab is expressed in the yeast *Pichia pastoris* and is composed of 378 amino acids. It is around a quarter of the size of conventional monoclonal antibodies.
In conjunction with selective inhibition of IL-17A and IL-17F, potential advantages that can differentiate sonelokimab from conventional monoclonal antibodies include its smaller size and albumin binding capacity. The smaller size of the sonelokimab nanobody compared with conventional monoclonal antibodies may enable differential deep tissue penetration. Furthermore, the albumin binding domain provides a mechanism for enrichment of sonelokimab at sites of chronic inflammation associated with edema and accumulation of albumin-rich fluid. Taken together, these characteristics are predicted to enable enhanced tissue penetration into HS lesions and impact on disease mechanisms. Drug tissue penetration is an important consideration in the treatment of HS, as disease presentation is often characterized by deep dermal morphologies (e.g. tunnels/fistulas) that are sites of inflammation and contribute to disease progression.

Study objective

Primary Objective:
1. To evaluate the efficacy of sonelokimab at 2 different dose levels (120 mg, 240 mg) compared with placebo in the treatment of participants with active moderate to severe hidradenitis suppurativa.

Secondary Objectives:
1. To evaluate the safety and tolerability of sonelokimab at 2 different dose levels (120 mg, 240 mg) compared with placebo in the treatment of participants with active moderate to severe hidradenitis suppurativa;

2. To assess the pharmacokinetics (PK) and immunogenicity of sonelokimab at 2 different dose levels (120 mg, 240 mg) in the treatment of participants with active moderate to severe hidradenitis suppurativa.

Exploratory Objective:
1. The exploratory objective is to assess biomarkers of participants with active moderate to severe hidradenitis suppurativa.

Study design

The planned study duration for individual participants will be up to 32 weeks, including a screening period of up to 4-weeks, 24-week treatment period, and a 4-week Safety Follow-up period.

This is a Phase 2 multi-center randomized, parallel-group, double-blind, placebo-controlled 2-part study evaluating the efficacy, safety, PK and

immunogenicity of sonelokimab in participants with active moderate to severe hidradenitis suppurativa (HS). The study includes adalimumab treatment as an active reference arm; however, no formal comparison of sonelokimab vs adalimumab is planned.

At the Screening Visit, each participant will provide informed consent, be assigned a unique participant number via the Interactive Response Technology (IRT), be assessed for eligibility with the inclusion and exclusion criteria and perform study activities as described in the protocol. Participants will undergo screening for up to 4 weeks before randomization to establish eligibility.

In Part A, eligible participants will be randomized (2:2:2:1) to receive either sonelokimab 120 mg or sonelokimab 240 mg, or matching placebo, or adalimumab up to Week 12. Participants randomized to adalimumab will receive 160 mg on Day 1 and 80 mg every 2 weeks up until Week 10. Randomization will be stratified by Hurley Stage status (II and III) and prior biologic use (yes/no).

The primary efficacy analysis will be performed at Week 12, comparing each of the sonelokimab treatment groups (sonelokimab 120 mg and sonelokimab 240 mg) versus placebo.

In Part B, participants who were initially randomized to sonelokimab 120 mg or 240 mg will continue treatment for the remainder of the study. Participants initially randomized to placebo will be re-randomized (1:1) to either sonelokimab 120 mg or 240 mg and will receive this treatment for the remainder of the study. Re-randomization will also be stratified by Baseline Hurley Stage status (II and III) and prior biologic use (yes/no at Screening).

Participants initially randomized to the adalimumab reference arm will be reallocated to treatment with sonelokimab 240 mg for the remainder of the study.

After the End of Treatment visit at Week 24, all participants will be followed for safety for additional 4 weeks, i.e., through Week 28.

Intervention

Test Product, Dose and Mode of Administration:

Sonelokimab will be presented as a prefilled syringe as sterile solution for subcutaneous (SC) injection.
Depending on the randomized treatment arm, participants in the sonelokimab treatment arms will receive either:
* Arm 1: sonelokimab 120 mg at Weeks 0, 2, 4, 6, 8, followed by injections every 4 weeks through Week 20;
at Weeks 10, 14, and 18 participants will receive placebo injections to maintain the blind;

* Arm 2: sonelokimab 240 mg at Weeks 0, 2, 4, 6, 8, followed by injections every 4 weeks through Week 20;
at Weeks 10, 14, and 18 participants will receive placebo injections to maintain the blind.

Depending on the randomized treatment arm, participants in the placebo or adalimumab arms will receive either:
* Arm 3: sonelokimab-matching placebo will be given as SC injection through Week 12, with injections at
Week 0, 2, 4, 6, 8, and 10.
o Sonelokimab-matching placebo will be presented as a prefilled syringe as sterile solution for SC injection.
o At the beginning of Part B at Week 12, participants in the placebo group will be re-randomized to one of the following 2 groups:
* Sonelokimab 120 mg at Weeks 12, 14, 16, 18, and 20;
* Sonelokimab 240 mg at Weeks 12, 14, 16, 18, and 20.

* Arm 4: adalimumab will be given as 160 mg at Week 0, followed by 80 mg once every 2 weeks; at Weeks 2, 4, 6, 8, and 10.
o Adalimumab will be presented as a prefilled syringe as sterile solution for SC injection.
o At the beginning of Part B at Week 12, participants in the adalimumab reference arm will be reallocated to receive sonelokimab 240 mg treatment for the remainder of the study at Weeks 12, 14, 16, 18, and 20.

Study burden and risks

Participation in this study may help generate future benefit for larger groups of patients with HS if sonelokimab proves to be successful in treating this disease to address an unmet medical need.

Sonelokimab has shown efficacy in 2 clinical studies in patients with psoriasis: a Phase 1 study (Study M1095-PSO-101) and a Phase 2 study (Study M1095-PSO-201). However, sonelokimab has not been studied in patients with HS and no direct benefit can be assumed.

The study has also been designed to minimize potential risks to participants. All subjects will undergo screening procedures aimed at reducing the likelihood and impact of any such risks. In addition, regular safety monitoring during the treatment period for all subjects will ensure that any
unanticipated effects of study participation are identified promptly and managed appropriately.

Potential Risks of Sonelokimab
In common with other potentially immune modulating agents, sonelokimab may increase the risk of infections, and adverse events (AEs) of infection have occurred in prior clinical studies with

sonelokimab. Blockade of the IL-17 pathway using monoclonal antibodies targeting IL-17A, IL-17A/F, or IL-17RA has been specifically associated with an increased risk of mucocutaneous
candida infections. Patients with active infection will be excluded from this study and any infections occurring during the study will be monitored as AEs. Candida infections will be
considered adverse events of special interest(AESIs).

Injection site reactions are a common finding with subcutaneously administered biologic therapies and have previously been observed in up to 3% of patients receiving sonelokimab. Injection site
reactions are readily detectable and usually manageable with standard treatments. Occurrence of injection site reactions will be monitored as AEs in this study.

All protein therapeutics have the potential to be immunogenic. Manifestations of systemic hypersensitivity may include anaphylaxis, pruritus, hypotension, serum sickness, or cutaneous
reactions. Events of pruritus and dermatitis have been reported in sonelokimab clinical studies. These events are not correlated with the development of anti-drug antibodies (ADA) to
sonelokimab. Potential hypersensitivity events will be monitored closely in this study and guidance on events where study treatment should be discontinued is given in the protocol.

IL-17 is proposed to play a role in maintaining the physiologic, healthy state of the intestinal mucosa. Blockade of the IL-17 pathway by mAbs to IL-17A, IL-17A/F, or the IL-17RA has been
associated with a potentially increased risk of inflammatory bowel disease. In clinical studies to date, no new cases of inflammatory bowel disease (IBD) have been associated with sonelokimab.

Events of diarrhea have been reported in Study M1095-PSO-201, at rates similar to the reference arm (secukinumab, IL-17A inhibiting mAb). Because diarrhea may occur as an early sign of
disruption of epithelial barrier integrity and intestinal immune homeostasis, diarrhea will be followed as AESI in this study.

Other safety topics evaluated for sonelokimab, but where a potential risk is not currently specifically identified are discussed in the sonelokimab investigator*s brochure (IB).

Contacts

Public
-

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Scientific
-

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. >=18 years of age.
2. Diagnosed with HS and has a history of signs and symptoms of HS dating back at least 6 months.
3. Total AN count (i.e., abscesses and/or inflammatory nodules) of >=5.
4. Subject has HS lesions present in >=2 distinct anatomical areas at least one of which must contain single or multiple fistulas (i.e., be Hurley Stage II or III);
5. Subject had an inadequate response to appropriate systemic antibiotics for treatment of HS (or demonstrated intolerance to, or had a contraindication to, systemic antibiotics for treatment of their HS).
6. Participants must a suitable candidate for treatment with adalimumab per approved local product information. If a chest X-ray or computed tomography (CT) for tuberculosis (TB) screening is required per local guidance, the X-ray or CT must have been taken within 3 months prior to the Screening.
7. If the subject is female, must be of non-childbearing potential or if of

childbearing potential, participant must agree to use highly effective methods of contraception.
8. Women of childbearing potential must have a negative serum human chorionic gonadotropin (hCG) pregnancy test at screening and a negative urine pregnancy test at Week 0/Day1 prior to the first administration of study treatment.
9. If male, participant must be willing to use a condom when sexually active with a partner of childbearing potential during the study and for 12 weeks after the last dose of study drug, unless surgically sterile.
10. Participant is considered reliable and capable of adhering to the protocol, visit schedule, or medication intake according to the judgment of the investigator.
11. Participant is able to understand and provide signed informed consent.

Exclusion criteria

1. Known hypersensitivity to sonelokimab, adalimumab or any of its excipients.
2. Draining fistula count of >=20.
3. Any other active skin disease or condition that may interfere with the assessment of HS.
4. Subject who currently use or plan used one or more prohibited treatments specified in this protocol.
5. Subjects enrolling in the non-antibiotic strata: use of systemic antibiotics for the treatment of HS within 28 days.
6. Previous exposure or subject in a study of brodalumab (anti-IL-17RA) and/or bimekizumab (anti-IL17 A/F).
7. Unsuitable for interleukin (IL)-17A therapy and anti-tumor necrosis factor alpha (TNFα) therapy.
8. Prior exposure to more than 2 biologic response modifiers.
9. Diagnosis of ulcerative colitis or Crohn's disease.
10. Subject has an active infection or history of infections.
11. Participant with evidence of tuberculosis infection (TB) at screening unless the following criteria apply:
i. A full TB work-up within 12 weeks establishes no evidence of active TB infection.
ii. Positive for latent TB per work-up must have completed sufficient treatment at least 4 weeks prior.
12. Any current nontuberculous mycobacterial (NTM) infection or any history of pulmonary NTM infection.
13. Concurrent acute or chronic viral hepatitis B virus (HBV) or hepatitis C virus (HCV) infection.
14. Evidence of human immunodeficiency virus (HIV) infection.
15. Tests positive for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection.
16. Concurrent malignancy or a history of malignancy during the past 5 years of with the following exceptions:

a. <=3 successfully excised or ablated, basal cell carcinomas of the skin.
b. One squamous cell carcinoma of the skin not worse than Stage T1 that has been successfully treated, with no signs of recurrence or metastases for at least the past 2 years.
c. Actinic keratosis.
d. Squamous cell carcinoma in situ of the skin successfully treated >6 months.
e. Localized carcinoma in situ of the cervix treated and considered cured.
17. History of a lymphoproliferative disorder including lymphoma or current signs and symptoms suggestive of lymphoproliferative disease.
18. Primary immunodeficiencies, prior splenectomy, or suppressive conditions, including subjects taking immunosuppressive therapy following organ transplants.
19. Had major surgery (e.g., hip replacement, aneurysm removal) within 6 months or is planning to have major surgery during the study.
20. History or concurrent clinically significant medical conditions or any other reason, including any physical, psychological, or psychiatric condition, that would compromise the safety or interfere with the subject's participation in the study, would make the participant an unsuitable candidate to receive study drug, or would put the participant at risk.
21. Has received live (including attenuated) vaccination within 8 weeks or planned during the study and up to at least 12 weeks after the last dose of study drug.
22. Has received Bacillus Calmette-Guérin vaccination within 1 year.
23. Presence of active suicidal ideation, or positive suicidal behavior; any history of suicidal attempt (including an actual attempt, interrupted attempt, or aborted attempt), or suicidal ideation in the past 6 months.
24. Presence of moderately severe depression or severe depression. Subjects are permitted to use 1 medication to treat depression provided dose is stable for 4 weeks prior. Subjects on multiple medications for depression are excluded from the study.
25. Severe cardiovascular comorbidities including history of myocardial infarction, unstable angina pectoris, stroke or heart failure New York Heart Association (NYHA) III or IV), or uncontrolled hypertension.
26. Clinically significant ECG abnormalities on centrally read ECG at the Screening.
27. Subject with laboratory abnormalities at the Screening.
28. Subject is enrolled in another interventional investigational study for a device or drug or has been so enrolled in the last 28 days prior or within 5 half-lives of the study drug prior to the Screening, whichever is longer.
29. Subject is pregnant or breastfeeding or plans to become pregnant while enrolled in the study and up to 12 weeks after the last dose of study drug;
30. History of chronic alcohol or drug abuse in the past year.
31. Subject is an employee, or direct relative of an employee, of the sponsor, at a study site, or of a third-party organization involved in the study.

Study design

Design

Study phase:	2
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):	01-11-2022
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	adalimumab
Generic name:	Humira®
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sonelokimab
Generic name:	Sonelokimab

Ethics review

Approved WMO

Date:	11-04-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	27-06-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-11-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2021-005928-38-NL
CCMO	NL80713.100.22