A randomized, subject and investigator blinded, placebo-controlled, multicenter study in parallel groups to assess the efficacy and safety of LYS006 in patients with moderate to severe inflammatory acne

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Primary objectiveTo assess the efficacy of LYS006 versus placebo on facial inflammatory lesion counts in patients with moderate to severe inflammatory acneSecondary objectiveTo assess the safety and tolerability of LYS006 in patients with moderate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Interventional

Summary

ID

NL-OMON50746

Source
ToetsingOnline

Brief title
CLYS006X2201

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
Acne

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: acne, LYS006

Outcome measures

Primary outcome

Baseline-adjusted total inflammatory facial lesion count at Week 12

Secondary outcome

Number and severity of adverse events

Study description

Background summary

Moderate to severe inflammatory acne is a debilitating disease, with visible inflammatory lesions on the face and subsequent risk of permanent scars. Available treatments are either associated with serious side effects (such as isotretinoin) or are modestly effective even after long term treatment (such as systemic antibiotics, oral zinc, and hormonal therapies). Acne is recognized as a chronic inflammatory skin disease, in which innate immunity play critical roles (Das and Reynolds 2014). Systemic antibiotics are associated with the rise of microbiological resistance and their long term use is more and more under critique, as most used tetracyclines are bacteriostatic rather than bactericidal and antibiotic resistance is a growing concern (Adler et al 2017). Thus, the development of a non-antibiotic, antiinflammatory and well-tolerated oral agent would respond to this medical need.

Zouboulis showed that in an open label Phase IIa clinical trial including 10 patients that treatment with the 5-LO inhibitor zileuton showed highly clinically relevant improvement of acne severity scores and reduction in inflammatory lesions (Zouboulis et al 2003, Zouboulis 2009). A multicenter placebo controlled study with 101 patients treated 4 times daily with 600 mg

zileuton for 12 weeks showed significant reduction in inflammatory lesions in the subset of patients with more severe acne (Critical Therapeutics 2005). This pointed to the potential implication of the leukotriene A4 hydrolase (LTA4H) pathway in acne and led to the proposal of testing a specific LTA4H inhibitor, LYS006, in moderate to severe inflammatory acne.

Study objective

Primary objective
To assess the efficacy of LYS006 versus placebo on facial inflammatory lesion counts in patients with moderate to severe inflammatory acne

Secondary objective
To assess the safety and tolerability of LYS006 in patients with moderate to severe inflammatory acne

Study design

This is a randomized, placebo-controlled, subject and investigator blinded, multicenter, non-confirmatory, parallel-group, proof-of-concept study in adult patients with moderate to severe facial inflammatory acne. After an initial screening period (up to 4 weeks), the study will be conducted over a treatment period of 11 weeks to evaluate the clinical efficacy of LYS006 versus placebo. Fifty- six patients will be randomized in a 3:1:3 ratio to one of the following treatment groups:
- Group 1: LYS006 capsules, high dose (20 mg BID)
- Group 2: LYS006 capsules, low dose (2 mg BID)
- Group 3: matching placebo (BID)
Within the three treatment groups, patients will be stratified by type of center (selected/non-selected for additional exploratory assessments) to enable interpretable exploratory analyses. As the selected centers will perform a broad range of exploratory assessments (enriched PK profiles, specific biomarkers assessments, optional biopsies, selfies), there is a need to have a sufficient number of patients enrolled in the LYS006 high dose and low dose groups. The stratification by type of centers level was chosen as it allows interpretation of analyses.

Exposure to placebo will be limited to a maximum of 11 weeks.

After treatment period completion, all patients will enter a post-treatment safety follow-up period of 4 weeks without study drug administration.
The maximum duration of study participation will be 20 weeks.

Intervention

LYS006 2 mg BID

LYS006 20 mg BID

Study burden and risks

Benefits
There is a chance that your acne will decrease. It is difficult to estimate this chance because it is a new product and because you might get the 'placebo'. In any case, the research provides valuable information for future treatments.

Cons
Blood will be taken from a vein of your arm with a small hollow needle, (so-called venipuncture) at every visit. Piercing of the vein can be painful and sometimes lead to a bruise. On study day 85 a cannula (a small tube) is inserted in a vein of your forearm once to facilitate the blood collection. In addition, skin biopsies are taken (optionally) at the beginning and end of the study (2x a biopsy of the acne skin and 1x a biopsy of healthy skin). A biopsy is the removal of a piece of tissue. Before the biopsy is taken, the skin will first be anesthetized locally with a prick. This prick gives a burning pain for a few seconds; you will not feel any pain after this injection.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

The patients eligible for inclusion in this study must fulfill all of the following criteria:
1. Written informed consent must be obtained before any assessment is performed.
2. Male and female subjects aged 18 to 45 years of age inclusive, and otherwise in good health as determined by medical history, physical examination, and vital signs. Electrocardiograms and laboratory tests should be consistent with normal values at screening.
3. Body weight between 50 and 120 kg, both inclusive, at screening.
4. Patients with papulo-pustular acne vulgaris (inflammatory acne):
- presenting at baseline with :
* 20 to 100 facial inflammatory lesions (papules, pustules and nodules),
* presenting at baseline and screening with
* no more than 2 facial inflammatory nodules or cysts,
* and a minimum of 10 non-inflammatory facial lesions (open and closed comedones)
- who are candidates for systemic treatment and for whom in the opinion of the investigator, an appropriate previous treatment with topical anti-acne medication :
* failed,
* or was not well tolerated,
* or is not indicated (e.g., due to large body surface area affected, e.g.,on the back)
5. Patients with Grade 3 (moderate) or Grade 4 (severe) IGA score confirmed by central
reading of standardized image capture (Visia® system) by an independent dermatologist
at screening and by the investigator*s clinical evaluation at baseline.
6. Able to communicate well with the investigator, to understand and comply with the requirements of the study.

Exclusion criteria

The patients fulfilling any of the following criteria are not eligible for inclusion in this study:
1. Previous treatment with investigational drugs at the time of screening, or

within 4 weeks or 5 half-lives of baseline, whichever is longer; or more as required by local regulations.
2. Previous treatment with any topical anti-acne therapy:
* prescription treatment within 2 weeks prior to baseline
* OTC within 1 week prior to baseline
The use of medicated anti-acne creams, medicated cleansers or medicated soaps is prohibited.
3. Previous treatment with any oral/systemic anti-acne therapy:
* oral antibiotics, dapsone, oral zinc within 4 weeks prior to baseline, retinoids, within 6 months prior to baseline and
* hormonal therapy (within 1 month prior to baseline.
If women of child bearing potential are using oral contraception, this contraception can be used under certain conditions.
4. Previous treatment with systemic corticosteroids or immunomodulators (e.g. cyclosporine, methotrexate, azathioprine) within 4 weeks prior to baseline.
5. Previous treatment with biologics (e.g anti-TNF* agents, anti-IL-1, or anti-IL-17) within 3 months or 5 half-lives (whichever is longer) prior to baseline.
6. Previous treatment with anti-IL-12/23 blocking agents (e.g. briakinumab and ustekinumab or p19 antibodies) within 6 months prior to baseline.
7. Previous surgical, physical (such as ThermaClear*), light (including blue or UV light, photodynamic therapy) or laser therapy within 4 weeks prior to baseline.
8. Previous facial treatment with medium depth chemical peels (excluding home regimens) within 3 months prior to baseline.
9. Concomitant medication(s) known to inhibit OAT3 or BCRP and that cannot be discontinued or replaced by safe alternative medication within 5 half-lives or 1 week (whichever is longer) to baseline and for the duration of the study.
10. Any other forms of acne.
11. Any severe, progressive or uncontrolled medical or psychiatric condition or other factors at randomization that in the judgment of the investigator prevents the patient from participating in the study.
12. Active systemic infections (other than common cold) within 2 weeks prior to baseline.
13. Subjects with eGFR <60 mL/min/1.73m2 at screening.
14. History or presence of crystals or stones in urine.
15. History or symptoms of malignancy of any organ system, treated or untreated, within the past 5 years.
16. Chronic infection with Hepatitis B or C.
17. History of auto-immune or immunodeficiency diseases, or a positive HIV test result at screening.
18. Pregnant or nursing women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test.
19. Women of child-bearing potential, unless they are using basic methods of contraception during dosing of study treatment.
20. Sexually active males must use a condom during intercourse while taking

drug and for 2 weeks after stopping study medication and should not father a child in this period.
21. History of drug abuse or unhealthy alcohol use.
22. Donation or loss of 400 ml or more of blood within 8 weeks prior to baseline, or longer if required by local regulation.
23. Inability or unwillingness to undergo repeated venipunctures.
24. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of drugs, or which may jeopardize the subject in case of participation in the study., Other protocol-defined exclusion criteria may apply.

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):	13-09-2018
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LYS006
Generic name:	LYS006

Ethics review

Approved WMO Date:	07-05-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-07-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-11-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-12-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	15-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	05-11-2020
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	EUCTR2017-003191-30-NL
ClinicalTrials.gov	NCT03497897
CCMO	NL65610.056.18