A randomized, placebo-controlled, evaluator-blinded, study to assess the anti-inflammatory effects of topical erythromycin and clindamycin in patients with inflammatory facial acne

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* To evaluate the effects of topically applied erythromycin and clindamycin in patients with facial AV* To explore skin and faecal microbiota in patients with AV;* To evaluate the effects of topically applied erythromycin and clindamycin on skin and...

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

Summary

ID

NL-OMON46405

Source
ToetsingOnline

Brief title
Anti-inflammatory effects of topical erythromycin and clindamycin in acne

Condition

- Epidermal and dermal conditions

Synonym
Inflammatory facial acne; Acne

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Cutanea Life Sciences and CHDR research budget

Intervention

Keyword: Anti-inflammatory, Clindamycin, Erythromycin, Facial acne

Outcome measures

Primary outcome

Efficacy endpoints

* Lesion count

* Investigator Global Assessment acne (IGA)

Pharmacodynamic endpoints

* Standardized facial photography by Canfield Visia and via selfie app

* Sebum measurements by Sebumeter®

* Perfusion by Laser Speckle Contrast Imaging (LSCI)

* Morphology by Optical Coherence Tomography (OCT)

* Local skin biopsy biomarkers (IL-1b, IL-1a, TNF-a IL-6, IL-12, IL-8, IL-10,

IL-17, IFN-g)

* Change in skin microbiota (16S NGS sequencing (lesional vs non-lesional))

* Change over time in p.acnes cultures

* Change over time in faecal microbiota

* Local skin surface biomarkers by TAP (IL-1a, IL-1b, TNF-a, IL-8, IL-10, IL-17)

Patient Reported Outcome (PRO)

* Subjective patient global assessment (sPGA)

Secondary outcome

N.A.

Study description

Background summary

Acne vulgaris (AV) is a cutaneous disease of the pilosebaceous follicles. In adolescents it is very common, the prevalence ranges from 35 to over 90% (1, 2). Acne vulgaris typically affects the face, neck, chest, upper back and upper arms. Clinical features include non-inflammatory lesions (closed and/or open comedos) and inflammatory lesions (papules, pustules and nodules). When becoming extensive, inflammatory lesions can lead to scarring and post-inflammatory hyperpigmentation and it is known that acne can have a significant impact on patients self-esteem and social life (3).
Four factors are involved in the pathophysiology of AV, i) follicular hyperkeratinisation, ii) increased sebum production, iii) Propionibacterium acnes (P. acnes) colonization within the follicle and iv) inflammation. The exact role of P. acnes in acne is an ongoing debate, however P. acnes is able to stimulate the immune system in several ways: stimulation of Toll-like receptors 2 and 4, direct stimulation of T lymphocytes, and the activation of the NRLP3-inflammasome via various NLRs, Figure 1 (4). Furthermore recent investigations suggest that the pro-inflammatory cytokine IL-1beta may play an important role in the development of inflammation in AV (5, 6).
Antibiotics including erythromycin (a macrolide antibiotic) and clindamycin (a lincosamide antibiotic) via topical and systemic administration route play a major role in the treatment of AV. Both erythromycin and clindamycin are bacteriostatic by reversibly binding to the P site on the 50S subunit of bacterial ribosomes. Furthermore, anti-inflammatory and immuno-modulating properties of these antibiotics have been described in vitro and in vivo, mostly in the field of respiratory medicine. A recent in-vitro study showed that erythromycin reduces IL-1beta in LPS stimulated PMBCs (7).
However, currently there is no mechanistic evidence of those anti-inflammatory properties in vivo in skin diseases such as acne. Therefore, the objective of this study is to assess the anti-inflammatory and immunomodulatory properties of topical erythromycin and clindamycin in patients with inflammatory acne.

Study objective

* To evaluate the effects of topically applied erythromycin and clindamycin in patients with facial AV

* To explore skin and faecal microbiota in patients with AV;
* To evaluate the effects of topically applied erythromycin and clindamycin on skin and faecal microbiota;

Study design

This is a randomized, open-label, placebo-controlled, evaluator-blinded study.

Intervention

Investigational drug
Erythromycin 4% topical gel formulation
Erythromycin is a bacteriostatic antibiotic that belongs to the macrolide group of antibiotics. Macrolides act as antibacterial by reversibly binding to the P site on the 50S subunit of bacterial ribosomes. A topical gel formulation with hyprolose and ethanol.
Clindamycin 1% topical lotion formulation:
Clindamcin is a bacteriostatic antibiotic that belongs to the lincosamide group of antibiotics. Lincosamides act as bacteriostatic by reversibly binding to the P site on the 50S subunit of bacterial ribosomes. An aqueous topical lotion formulation with ethanol.
Comparative drug
Seventy (70) % topical ethanol solution will serve as placebo.

Study burden and risks

The overall aim of this study is to evaluate the anti-inflammatory and immunomodulatory properties of topical erythromycin and clindamycin in acne patients. Treatment with topical erythromycin and clindamycin is known to be safe and well tolerated. We refer to the SmPC in D2. of the submission dossier for more information. Two (2) mm biopsies will be taken from a facial lesion, this is minimal invasive with a rapid healing and low risk of scarring and therefore justified.

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

1. Healthy male and female subjects, 18 to 45 years of age. The health status is verified by absence of evidence of any clinical significant active or uncontrolled chronic disease other than AV following a detailed medical history, a complete physical examination including vital signs, 12-lead ECG, hematology, blood chemistry, virology and urinalysis;
2. Mild to moderate inflammatory acne vulgaris on the face, *5 inflammatory lesions (papules and/or pustules), present at screening and baseline visit
3. A maximum of 5 nodules present at screening and baseline visit
4. Inflammatory acne present for at least 6 months
5. Fitzpatrick skin type I-II (Caucasian)
6. Able and willing to give written informed consent and to comply with the study restrictions.
7. Willing to comply with 2x2mm facial skin punch biopsies

Exclusion criteria

1. Severe acne where systemic treatment is needed
2. Use of any topical (anti-acne) medication (prescription or OTC) within 2 weeks prior to baseline
3. Use of any oral/systemic treatment for acne, including oral antibiotics, excluding OAC, within 4 weeks prior to baseline
4. Use of systemic isotretinoin within 6 months prior to baseline
5. History of pathological scar formation (keloid, hypertrophic scar)
6. Known hypersensitivity to erythromycin or clindamycin, drugs of the same class, or any of their excipients.

7. Known contact dermatitis reaction to any product
8. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrollment.
9. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year.
10. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening
11. Pregnant, a positive pregnancy test, intending to become pregnant, or breastfeeding

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-12-2017
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	Clindamycin 1% topical lotion formulation
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NA

Generic name:	Erythromycin 4% topical gel formulation

Ethics review

Approved WMO Date:	06-12-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-12-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-02-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2018
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	EUCTR2017-3105-18-NL
CCMO	NL62760.056.17