A randomized, double-blind, vehicle-controlled trial with safety run-in to assess the safety, tolerability and efficacy of DLQ02, a novel topical formulation Cyclosporine A (CsA), applied twice daily over four weeks to patients with plaque psoriasis.

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To assess the safety, tolerability, pharmacodynamics and efficacy of two DLQ02 topical formulations in patients with plaque psoriasis. To assess systemic exposure of CsA and F6H8 after topical application.

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

Summary

ID

NL-OMON51426

Source
ToetsingOnline

Brief title
DLQ02 in patients with plaque psoriasis

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
Plaque Psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: Dermaliq Therapeutics Inc.
Source(s) of monetary or material Support: Dermaliq Therapeutics Inc.

Intervention

Keyword: Cyclosporin A, Plaque Psoriasis

Outcome measures

Primary outcome

Tolerability / safety endpoints

1) Adverse events (AE)

2) Laboratory safety testing (blood and urine)

3) 12-lead ECGs

4) Vital signs

5) Physical examination

6) Systemic levels of CsA and the novel excipient F6H8

7) Skin irritation of non-lesional skin by local irritation grading scale

(LIGS) (Part A only)

Adherence

Electronic diary with photo capture function to monitor treatment compliance.

Secondary outcome

Pharmacokinetic endpoints

1) Cutaneous PK in skin biopsies.

2) Systemic levels of CsA and the novel excipient F6H8

Pharmacodynamic and efficacy endpoints

1) Severity of psoriasis target lesion after 1, 2, 3 and 4 weeks of treatment using clinical assessment of signs (erythema, induration, scaling) expressed as TSS (Total Sum Score)

2) Percent of patients achieving clinical scores of the target lesion of clear (score of 0 for each symptom) or almost clear (erythema, induration and scaling each <=1) at week 4.

3) Score for individual symptoms of the target lesion (erythema, induration and scaling) after 1, 2, 3 and 4 weeks of treatment

4) Target lesion area assessed by 2D photography analysis after 1, 2, 3 and 4 weeks of treatment

5) Target lesion erythema assessed by multispectral/3D photography after 1, 2, 3 and 4 weeks of treatment

6) Target lesion roughness assessed by multispectral/3D photography after 1, 2, 3 and 4 weeks of treatment

7) Patient reported itch of the target lesion (twice daily NRS by e-diary) after 1, 2, 3 and 4 weeks of treatment

8) Target lesions thickness assessed by Optical Coherence Tomography (OCT) (lesional and non-lesional) after 1, 2, 3, and 4 weeks of treatment.

9) Microcirculation of the target lesion assessed by Laser Speckle Contrast Imaging (LSCI) after 1, 2, 3 and 4 weeks of treatment

10) Skin surface biomarkers by FibroTX Patch, after 1, 2, 3 and 4 weeks of treatment

11) Transepidermal water loss assessed by Aquaflux and GPskin, after 1, 2, 3,

4, weeks of treatment.

12) Skin pH assessed by Courage and Khazaka pH meter after 1,2,3, and 4 weeks of treatment.

13) Digital PASI score assessed with total body photography at baseline, end of treatment and at end of study.

Study description

Background summary

Psoriasis is a common skin disorder affecting up to an estimated 3% of the world*s population. The most prevalent form of psoriasis, psoriasis vulgaris or plaque psoriasis, is characterized by the presence of sharply demarcated erythematous plaques covered with white scales. These lesions can occur all over the body but are most often seen on the extensor surface of the joints, nether regions and on the scalp. Patients can experience excessive itch, pain and sometimes bleeding of the lesions. Moreover, the visual appearance of psoriatic lesions can severely impact the patients* psychological state and quality of life (Boehncke and Schön, 2015).
An abundancy of different factors contributes to the pathogenesis of psoriasis. However, aberrant activation of inflammatory pathways in the skin are thought to be the underlying cause. Excessive infiltration of immune (T)-cells in the skin and their interactions with cutaneous resident immune cells results in the hyperproliferation of keratinocytes and subsequent thickening of the epidermis. Because of the importance of the inflammatory reaction in the pathogenesis of psoriasis, one of the treatments that can be prescribed is the immunosuppressive drug Cyclosporine A, a calcineurin inhibitor. Cyclosporine A (CsA) is a cyclic polypeptide with a strong immunosuppressive effect by reversibly blocking T-cell proliferation. Currently CsA is available only as an oral solution. The side effect profile of CsA includes nausea, hypertension and nephrotoxicity, of which the latter can be irreversible. A topical CsA drug product would have great advantage in the treatment of psoriasis, as the drug will be applied directly to the target tissue and it is expected that there will be no or only minimal systemic exposure. This concept has been investigated in previous studies, however none of these investigations were successful in delivering Cyclosporine across the stratum corneum.
Dermaliq has developed a novel topical drug product candidate of CsA: DLQ02, a liquid formulation with the target to facilitate dermal delivery of the active compound to the target tissues.
In this phase I/IIa study the safety, tolerability, pharmacodynamics and

efficacy of two dose strengths of DLQ02 will be assessed when applied BID to one target lesion for four weeks in 36 patients with plaque psoriasis.

Study objective

To assess the safety, tolerability, pharmacodynamics and efficacy of two DLQ02 topical formulations in patients with plaque psoriasis.
To assess systemic exposure of CsA and F6H8 after topical application.

Study design

Phase I/IIa, single-centre, randomized, double-blind, vehicle-controlled study with a safety run-in period. The study will entail two parts. The aim of part A is to closely observe the safety through daily assessments of both the lesional and non-lesional skin whereas Part B is only focussing on lesional skin.

Intervention

DLQ02 is a liquid topical drug product with CsA as active. In this study two Cyclosporine concentrations (0.2% and 1.0%) will be assessed.

Study burden and risks

DQL02 is expected to have a local immunosuppressive effect associated with the active ingredient CsA. The risks associated with the topical administration of DQL02 to humans have not yet been identified, because this compound has not yet been applied to the skin of humans. However, the effect of the excipient F6H8 on the eye has been studied in 5 clinical trials, and has shown excellent in-use tolerability. The eye itself is extremely sensitive to irritating substances and following the application of drops to the eye there is often smearing to the sensitive skin around the eye. Therefore, the ocular safety of F6H8 is considered a sensitive indicator for irritation that may occur following topical administration of F6H8 to the skin. Risks associated with systemic CsA treatment are amongst others nephrotoxicity and hypertension. This is not expected with DLQ02 as systemic exposure is unlikely and the maximum dose is 29 times lower than the maximum allowed dose for systemic cyclosporine.

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

Patients must:
1) Be males or non-pregnant, non-lactating females.
2) Be at least 18 years of age at time of consent.
3) Have stable psoriatic plaque psoriasis (for >= 6 months), as confirmed by the patient.
4) Have a maximum (treatable) BSA of 2.5% (only part B)
5) Have a target plaque (area) suitable for treatment >=15cm2 and <=100cm2 with a severity defined by TSS score >= 4, with at least a clinical score of >= 2 for either erythema or induration and >=1 for the symptom scaling.
6) Be able and willing to follow instructions and comply with the study restrictions, including participation in all trial assessments and visits.
7) Provide written informed consent.
8) Be willing to refrain from medications for psoriasis according to the wash-out periods.
9) Patients and their partners of childbearing potential must use effective contraception, for the duration of the study and for 3 months after the last dose.

Exclusion criteria

Patients must not:
1) Have any current and / or recurrent clinically significant skin condition which will interfere with the clinical findings of the study as assessed by the investigator.
2) Have a current diagnosis of psoriasis other than plaque psoriasis (including guttate psoriasis, psoriasis erythroderma and pustular psoriasis).
3) Use the following psoriasis medications. Wash-out periods are stated below.
• Local treatment of plaques with anti-psoriatics (e.g., vitamin D analogs, corticosteroids, retinoids, tacrolimus or other calcineurin inhibitors excepting CsA (prohibited): 2 weeks prior to baseline.
• Emollients or scale-softening treatments on target plaques (including salicylic acid): from baseline onwards.
4) Have a current systemic treatment with psoriasis medication (e.g. retinoids and immunomodulating drugs such as methotrexate and tacrolimus, CsA or a treatment with biologic.)
5) Begin treatment with systemic or locally acting medications which might counter or influence the study aim (e.g., medications which are known to provoke or aggravate psoriasis including but not limited to antimalarial drugs, beta-blockers [e.g., propanolol], lithium, iodides, angiotensin-converting enzyme inhibitors, nifepidine, indomethacin, ciprofloxacin, and diphenhydramine) prior to baseline (therapy with stable dose is allowed).
6) Begin treatment with CYP3A4 interactive drugs [e.g., miconazole, ketoconazole, erythromycin, clarithromycin, diltiazem, ritonavir, verapamil, grapefruit].
7) Have history of PUVA if >1000 J/cm2 or >200 cumulative treatments.
8) Have participated in a clinical research trial within 90 days, or 5 half-lives of the investigational product, whichever is greater, prior to screening visit.
9) Be study site employees, or immediate family members of a study site or sponsor employee.
10) Have prolonged exposure to UV light within two weeks prior to study day 1 or intention to have such exposures during the study.
11) Have a history of drug abuse within the past two years.
12) Regular alcohol consumption in males >21 units per week and females>14 units per week (1 unit approximately 240 ml of beer, 25 ml of 40% spirit or a 125 ml glass of wine), or a history of alcohol abuse within the past two years.
13) Change smoking habits during the 4 weeks prior to study start or during the study; smokers are allowed up to 6 cigarettes per day if smoking is a current habit.
14) Have clinically significant abnormal biochemistry, hematology or urinalysis as judged by the investigator.
15) Have liver function tests (ALT, AST, GGT, ALP) range >2.5 X upper limit of normal of each parameter at screening.
16) Have a clinically significant abnormal renal function (including any stage

of chronic kidney disease).
17) Have positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab), or human immunodeficiency virus (HIV) results.
18) Have live vaccination during the study or in the 2 weeks before study start.
19) Have vaccination for SARS-CoV-2 within 14 days prior to initial dosing, or planned during the course of the study.
20) Have history of malignancy, except adequately treated non-invasive skin cancer (basal or squamous cell carcinoma).
21) Have clinically significant illness or infection that may, in the opinion of the investigator, contraindicate participation in the trial or interfere with the outcome of the trial in the 4 weeks before the baseline visit and during the trial.
22) Have history of sensitivity to any of the study medications, or components thereof, or a history of drug or other allergy that, in the opinion of the investigator or medical monitor, contraindicates participation.
23) Have clinically significant uncontrolled hypertension as judged by the investigator (stable treatment is allowed).
24) Fail to satisfy the investigator of fitness to participate in the trial for any other reason.
25) Have loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening.
26) Have used Evotears® or Novatears® one week before Day 1 or plan to use it during the course of the trial

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):	01-07-2022
Enrollment:	36

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	DLQ02
Generic name:	Cyclosporin

Ethics review

Approved WMO Date:	14-04-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-06-2022
Application type:	First submission
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:	16-02-2023
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	EUCTR2022-001071-13-NL
CCMO	NL80977.056.22