Clinical trial results:
Assessing the efficacy of image-guided laser-assisted Enstilar® delivery for treatment of psoriatic nails - a proof-of-concept, single-center, prospective, open-label, randomized, clinical trial with an intra-individual comparison of treatments

Summary

EudraCT number	2019-002960-29
Trial protocol	DK
Global end of trial date	09 September 2021

Results information

Result version number	v1 (current)
This version publication date	30 June 2022
First version publication date	30 June 2022

Trial information

Trial identification

Sponsor protocol code	79048

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04580537
WHO universal trial number (UTN)	-
Other trial identifiers	Danish Data Protection Agency: P-2020-500, Danish Ethics Committee: 79048/H-19047222

Notes:

Sponsors

Sponsor organisation name	Copenhagen University Hospital
Sponsor organisation address	Nielsine Nielsens Vej 17, entrance 9, 2nd floor, Copenhagen NV, Denmark, 2200
Public contact	Prof. Merete Hædersdal, MD PhD DMSc, Copenhagen University Hospital, Bispebjerg Department of Dermatology [D92], +45 24 45 43 93, mhaedersdal@dadlnet.dk
Scientific contact	Prof. Merete Hædersdal, MD PhD DMSc, Copenhagen University Hospital, Bispebjerg Department of Dermatology [D92], +45 24 45 43 93, mhaedersdal@dadlnet.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2021
Global end of trial reached?	Yes
Global end of trial date	09 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy of Enstilar for treatment of nail psoriasis using laser pretreatment

Protection of trial subjects:

Pliapel 70 mg/g + 70 mg/g creme lidocaine + tetracaine, Air chiller device, Image-guided laser-treatment to avoid damage to nail matrix/nail bed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 August 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	11
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment initiated: 25-September-2020
Last patient last visit: 01-June-2021
End of study: 18-November-2021
Patients were recruited via social media and at the Department of Dermatology at the Copenhagen University Hospital, Bispebjerg, in Denmark.

Pre-assignment

Screening details:

We assessed the following during the screening phase: clinical history of psoriasis/psoriatic arthritis, signs of nail psoriasis, no other skin or nail disease that may affect the treatment outcome, willingness to use a smartphone app to collect images for remote assessment throughout the study period

Period 1

Period 1 title	Treatment and follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Blinding not possible due to intrapatient controlled design and use of an ablative laser

Arms

Are arms mutually exclusive?	No
Arm title	AFL + Enstilar

Arm description:

Ablative fractional laser pretreatment + topical Enstilar (Calcipotriol/Betamethasone) foam treatment

Arm type	Experimental
Investigational medicinal product name	Enstilar (Calcipotriol/Betamethasone Dipropionate Aerosol Foam)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous foam
Routes of administration	Cutaneous use

Dosage and administration details:

Direct application of Enstilar foam to psoriatic finger and/or toe nails to create a thin even layer; once daily for 24 weeks; no occlusion

Arm title	Enstilar

Arm description:

Topical Enstilar (Calcipotriol/Betamethasone) foam treatment

Arm type	Active comparator
Investigational medicinal product name	Enstilar (Calcipotriol/Betamethasone Dipropionate Aerosol Foam)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous foam
Routes of administration	Cutaneous use

Dosage and administration details:

Direct application of Enstilar foam to psoriatic finger and/or toe nails to create a thin even layer; once daily for 24 weeks; no occlusion

Number of subjects in period 1	AFL + Enstilar	Enstilar
Started	11	11
Completed	10	10
Not completed	1	1
Physician decision	1	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment and follow-up

Reporting group description: -

Reporting group values	Treatment and follow-up	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	47		
inter-quartile range (Q1-Q3)	35.5 to 57.5	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	7	7	

Subject analysis sets

Subject analysis set title	AFL + Enstilar
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Half of all psoriatic nails (per patient) received ablative fractional laser pre-treatment and topical treatment

Subject analysis set title	Enstilar
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Half of all psoriatic nails (per patient) received only received topical treatment

Reporting group values	AFL + Enstilar	Enstilar	
Number of subjects	11	11	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
median	47	47	
inter-quartile range (Q1-Q3)	35.5 to 57.5	35.5 to 57.5	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	7	7	

End points

End points reporting groups

Reporting group title	AFL + Enstilar
Reporting group description:	
Ablative fractional laser pretreatment + topical Enstilar (Calcipotriol/Betamethasone) foam treatment	
Reporting group title	Enstilar
Reporting group description:	
Topical Enstilar (Calcipotriol/Betamethasone) foam treatment	
Subject analysis set title	AFL + Enstilar
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Half of all psoriatic nails (per patient) received ablative fractional laser pre-treatment and topical treatment	
Subject analysis set title	Enstilar
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Half of all psoriatic nails (per patient) received only received topical treatment	

Primary: Reduction in N-NAIL score

End point title	Reduction in N-NAIL score
End point description:	
End point type	Primary
End point timeframe:	
Baseline vs end of trial (week 24)	

End point values	AFL + Enstilar	Enstilar		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: 0-300	28	19		

Statistical analyses

Statistical analysis title	Paired t-test
Statistical analysis description:	
Tested for normality using Shapiro-Wilk normality test, evaluated using Bonferroni-corrected multiple paired-t tests, p-values less than 0.05 were considered significant	
Comparison groups	AFL + Enstilar v Enstilar

Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority[1]
P-value	= 0.62
Method	t-test, 2-sided

Notes:

[1] - No significant difference between groups but significant improvement (p=0.01) at end of trial for both groups compared to baseline

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs are reported within 24 hours to sponsor-investigator Merete Hædersdal. At the end of the trial, a final report with all AEs, ARs, SAEs, and SUSARs was submitted to DKMA and the IRB

Adverse event reporting additional description:

The investigators were responsible for routine assessments of AEs and ARs. All clinical complaints, signs or symptoms that meet AE or AR definitions were documented in the study record and the participant's medical record.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Adverse events

Reporting group description:

All subjects experienced mild local skin reactions to the topical treatment and the laser pretreatment.

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Injury, poisoning and procedural complications			
Laser therapy	Additional description: Persistent post-laser erythema (fully recovered by end of trial)		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Nail disorder	Additional description: Onychocryptosis (not treatment-related, fully recovered by end of trial)		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pain of skin	Additional description: Transient application site pain (fully recovered by end of		

	trial)		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Paronychia	Additional description: Acute nail fold infection affecting two toes due to improper nail care (not treatment related, fully recovered by end of trial)		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Local reaction	Additional description: Mild local and nail reactions related to topical and/or laser treatment including erythema, swelling, crusting, erosion, flaking, skin peeling, onychoschizia, hyperpigmentation (all fully recovered by end of trial)		
subjects affected / exposed	11 / 11 (100.00%)		
occurrences (all)	11		
Musculoskeletal and connective tissue disorders			
Pain in extremity	Additional description: Transient proximal interphalangeal joint pain (not treatment-related, fully recovered by end of trial)		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscular weakness	Additional description: Transient reduction in grip strength (not treatment-related, fully recovered by end of trial)		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2020	Due to Covid-19, an amendment to prevent further delays was necessary. The main changes were: -Request to include social media for recruitment -Extension of the trial period -Healthcare smartphone app (picture collection time point) -Inclusion of finger and toenails to reach recruitment goal
07 April 2021	Due to Covid-19, a 2nd amendment was necessary to finalize the study. The main changes were: -Request to extend visit window (+/-3 weeks) -Reduced number of patients from 25 to 11 -Extension of the trial period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Small sample size, short follow-up, no rheumatological baseline screening, hybrid trial design with no prior published evidence on remote assessment of AE in a nail psoriasis context

Notes: