EU Clinical Trials Register

Clinical trial results:

Impact of thermo-mechanical intervention on Protoporphyrin IX accumulation and biodistribution in normal skin following topical 5-aminolevulinic acid at high and low vehicle viscosity

Summary

EudraCT number	2018-004397-96
Trial protocol	DK
Global end of trial date	27 November 2019

Results information

Result version number	v1 (current)
This version publication date	10 October 2020
First version publication date	10 October 2020

Trial information

Trial identification

Sponsor protocol code	CF20112018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04221126
WHO universal trial number (UTN)	-
Other trial identifiers	Ethics Committee of the Capital Region of Denmark: H-1900394, Danish Medicine Agency: 2018-004397-96

Notes:

Sponsors

Sponsor organisation name	Bispebjerg Hospital
Sponsor organisation address	Nielsine Nielsens Vej 17, building 9, 2. Floor, Copenhagen NV, Denmark, 2400
Public contact	Merete Haedersdal, Katrine Togsverd-Bo, Camilla Foged, Department of Dermatology, +45 38636173, camilla.foged.01@regionh.dk
Scientific contact	Merete Haedersdal, Katrine Togsverd-Bo, Camilla Foged, Department of Dermatology, +45 38636173, camilla.foged.01@regionh.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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2019
Global end of trial reached?	Yes
Global end of trial date	27 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We aimed to explore TMFI pretreatment before ALA incubation with cream and gel vehicles And quantify PpIX fluorescence at the skin surface and inside skin.

Protection of trial subjects:

Biopsies were sampled under local anesthesia with 2 ml Lidocaine with adrenaline (Lidocain with adrenalin, SAD) 20 mg/ml+5mikrog/ml adrenaline and 20 mg/ml+5mikrog/ml lidocaine. Pain during pretreatment with TMFI were evaluated on an numeric scale.

Background therapy:

Non treatments that are not test or comparator

Evidence for comparator:

ALA was dissolved in a a cream-vehicle and a gel-vehicle . The rationale behind this was that hydrophilic drugs (e.g. ALA) was dissolved in a low viscosity liquid-based vehcle may be more readily distributed within the skin compared to drugs dissolved in a high viscosity vehicle.

Actual start date of recruitment	29 April 2019
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	16

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The participants will be recruited through the website www.forsoegsperson.dk, announcement in MOK (Mediciner Organisationernes Kommunikationsorgan) and on their Facebook page, announcement in the Facebook group "Medicin – Københavns Universitet" and notices at Bipsebjerg Hospital and Panum Instituttet.

Pre-assignment

Screening details:

Screening criteria: Healthy, above 18 years, Fitzpatrick I-III and normal skin on the upper back, fertile women w/ negative U-hCG and w/ use of safe anticontraceptive during the entire study period.
32 participants screened for inclusion, 16 included. Excluded due to folliculitis, acne etc on the upper back.

Pre-assignment period milestones

Number of subjects started	16
Number of subjects completed	16

Period 1

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

Blinding implementation details:

Randomization will be conducted with consecutively numbered closed, non-transparent envelopes containing a computer-generated allocation to specific test areas. The envelopes will be taken to use in numeric order and will be opened at the day of inclusion. Participants are non-blinded. Investigators are non-blinded in the clinical evaluation. A blinded investigator will evaluate the microscopy.

Arms

Are arms mutually exclusive?	No
Arm title	TMFI pretreatment + cream

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Gliolan
Investigational medicinal product code	PDL506
Other name	5-aminolevulinic acid
Pharmaceutical forms	Cream, Gel
Routes of administration	Topical use

Dosage and administration details:

125 uL per test area

Arm title	No pretreatment + gel

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Gliolan
Investigational medicinal product code	PD L 506
Other name	5-aminolevulinic acid
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

125 uL per test area

Arm title	No pretreatment + cream
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Gliolan
Investigational medicinal product code	PDL506
Other name	5-aminolevulinic acid
Pharmaceutical forms	Cream
Routes of administration	Topical use
Dosage and administration details:	
125 uL per test area	
Arm title	TMFI pretreatment + gel
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Gliolan
Investigational medicinal product code	PDL506
Other name	5-aminolevulinic acid
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

125 uL per test area

Number of subjects in period 1	TMFI pretreatment + cream	No pretreatment + gel	No pretreatment + cream
Started	16	16	16
Completed	16	16	16

Number of subjects in period 1	TMFI pretreatment + gel
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Intervention (overall period)

Reporting group description:

Pre-study (Study A) including 4 participants and the actual study (Study B) including 12 participants.

Reporting group values	Intervention (overall period)	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
adults	16	16	
Gender categorical Units: Subjects			
Female	8	8	
Male	8	8	

End points

End points reporting groups

Reporting group title	TMFI pretreatment + cream
Reporting group description: -	
Reporting group title	No pretreatment + gel
Reporting group description: -	
Reporting group title	No pretreatment + cream
Reporting group description: -	
Reporting group title	TMFI pretreatment + gel

Reporting group description: -

Primary: PpIX fluorescence at skin surface photometer

End point title	PpIX fluorescence at skin surface photometer

End point description:

End point type	Primary

End point timeframe:

Skin surface PpIX fluorescence fotos + photometer from baseline - 3 hours.

End point values	TMFI pretreatment + cream	No pretreatment + gel	No pretreatment + cream	TMFI pretreatment + gel
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	16
Units: AU				
median (inter-quartile range (Q1-Q3))	52 (41 to 63)	20.5 (13 to 35)	43.5 (28 to 52)	36 (24 to 49)

Statistical analyses

Statistical analysis title	Wilcoxon
Comparison groups	TMFI pretreatment + gel v No pretreatment + cream v No pretreatment + gel v TMFI pretreatment + cream
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: PpIX fluorescence at skin surface photos

End point title	PpIX fluorescence at skin surface photos

End point description:

End point type	Primary

End point timeframe:
From baseline until 3 hours.

End point values	TMFI pretreatment + cream	No pretreatment + gel	No pretreatment + cream	TMFI pretreatment + gel
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	16
Units: AU				
median (inter-quartile range (Q1-Q3))	7848 (4285 to 12836)	3723 (1722 to 5449)	5441 (2612 to 8235)	4591 (3821 to 7398)

Statistical analyses

Statistical analysis title	Wilcoxon
Comparison groups	TMFI pretreatment + cream v No pretreatment + gel v No pretreatment + cream v TMFI pretreatment + gel
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From study start until 14 days after study day.	
Assessment type	Non-systematic

Dictionary used

Dictionary name	SUSARs
Dictionary version	1

Reporting groups

Reporting group title	All participants

Reporting group description: -

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (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	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)		
Skin and subcutaneous tissue disorders			
Hyperpigmentation	Additional description: At day 14 follow-up, two participants developed mild post-inflammatory hyperpigmentation in all ALA-test areas that was unrelated to TMFI exposure		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

normal skin on the back opposed to thin facial skin or diseased skin with localized hyperkeratoses, TMFI settings

Notes: