Clinical trial results:
Multimodal optical imaging for pretreatment evaluation for cutaneous microparticle delivery

Summary

EudraCT number	2017-002975-25
Trial protocol	DK
Global end of trial date	20 December 2019

Results information

Result version number	v1 (current)
This version publication date	02 May 2020
First version publication date	02 May 2020

Trial information

Trial identification

Sponsor protocol code	59325

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bispebjerg Hospital
Sponsor organisation address	Bispebjerg Bakke 23, Kbh N, Denmark,
Public contact	Dermatologisk forskningsafdeling, Bispebjerg Hospital, 0045 41184700, merete.haedersdal@regionh.dk
Scientific contact	Dermatologisk forskningsafdeling, Bispebjerg Hospital, 0045 41184700, merete.haedersdal@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	30 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 July 2018
Global end of trial reached?	Yes
Global end of trial date	20 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To investigate the utility of RCM and OCT to assess micromorphology and gold microparticle delivery in acne skin after 6 weeks of topical treatment with adapalene-benzoyl peroxide (A-BPO).

Protection of trial subjects:

Before application of didoe laser pulses subjects had to precool the test sites with ice. If participatns experienced erythema and/or pain during A-BPO treatment they were advised to pause the treatment for up to two days.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark and private dermatological practices in Copenhagen, Denmark. Further, patients were recruited from social media.

Pre-assignment

Screening details:

Patients were screened if they seemed to meet the inclusion criteria.

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	One arm
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Adapalene- Benzoyl Peroxide
Investigational medicinal product code	
Other name	Epiduo
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Patients were instructed to apply A-BPO gel once daily in the facial area from baseline (after first imaging session) until 3 days before the week 6 visit.

Number of subjects in period 1	One arm
Started	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	15	15	
Age categorical			
18-45			
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
18-45	15	15	
Age continuous			
Units: years			
arithmetic mean	22.3		
standard deviation	± 2.7	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	5	5	

Subject analysis sets

Subject analysis set title	Morphological changes
Subject analysis set type	Full analysis

Subject analysis set description:

Morphological characteristics of hair follicles were evaluated in RCM images.
Median infundibulum diameter, um: Week 0 63um, Week 3 57um, Week 6 54um
Follicle border, dark grey: Week 0: 60.1%, Week 3 91.4%, Week 6: 88.5%
Follicle border, hyperreflective: Week 0: 39.9%, Week 3: 8.6%, Week 6: 11.5%
Follicle content, empty: Week 0 59.8%, Week 3: 72.9%, Week 6: 80.3%
Follicle content, amorphous grey: Week 0: 25.1%, Week 3: 17.4%, Week 6: 11.8%
Follicle content, hyperreflective: Week 0: 15.1%, Week 3: 9.7%, Week 6: 7.9%
Thickened border: Week 0: 46.7%, Week 3: 28.6%, Week 6: 23.4%

OCT characteristics
Epidermal Thickenss, median, um: Week 0: 85.9 um, Week 6: 102.3 um
Blood flow (speckle variance): Week 0: 0.15, Week 6: 0.18

Subject analysis set title	Gold microparticle analyses
Subject analysis set type	Full analysis

Subject analysis set description:

RCM: Number of hair follicles with hyperreflective content were evaluated before and after gold microparticle (GMP) application in epidermis, dermoepidermal junction (DEJ) and dermis week 0 and week 6.
Week 0
Epidermis: Before GMP: 6%, after GMP: 89%
DEJ: Before GMP: 7%, after GMP 74%
Dermis: Before GMP 6 follicles, after GMP 13 follicles

Week 6
Epidermis: Before GMP: 9%, after GMP: 85%
DEJ: Before GMP: 5%, after GMP 76%
Dermis: Before GMP 3 follicles, after GMP 14 follicles

OCT
GMP penetration depth week 0: 206 um
GMP penetration depth week 6: 291 um

Reporting group values	Morphological changes	Gold microparticle analyses	
Number of subjects	15	15	
Age categorical			
18-45			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
18-45	15	15	
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	5	5	

End points

End points reporting groups

Reporting group title	One arm
Reporting group description: -	
Subject analysis set title	Morphological changes
Subject analysis set type	Full analysis

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OCT
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Primary: Morphological changes

End point title	Morphological changes

End point description:

The study was designed as an exploratory study with no formal statistical sample size calculation. Fifteen patients with acne and a total of 945 hair follicles were considered sufficient to investigate the effect of A-BPO on hair follicle and skin morphology. Non-parametric statistics were used for morphological changes, and changes in epidermal thickness and blood flow measurements. Descriptive data were presented with medians and interquartile ranges (IQR). Chi square test was applied on hair follicle characteristics. Mann Whitney U was applied to test differences in hair follicle diameters between facial sites at Week 0 and Week 6. Spearman correlation coefficient was calculated to test the association between GMP penetration depth and epidermal thickness in OCT images.

End point type	Primary

End point timeframe:

6 weeks

End point values	One arm	Morphological changes		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: Percentage	15	15		

Attachments (see zip file)	Table 1/Table 1.pdf

Statistical analyses

Statistical analysis title	Statistical analyses morphological changes
Comparison groups	One arm v Morphological changes
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Median difference (net)

Primary: Gold microaparticle delivery

End point title	Gold microaparticle delivery

End point description:

Descriptive statistics is presented as medians and interquartile ranges (IQR). Due to the intra-individual study design, we paired data. Hence, Wilcoxon Signed Rank test of matched pairs was applied on number of follicles and eccrine ducts with hyperreflective content before and after GMP application before and after treatment with A-BPO. P values <0.05 were considered significant and all tests were two-sided.

End point type	Primary

End point timeframe:

6 weeks

End point values	One arm	Gold microparticle analyses		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: percentage	15	15		

Attachments (see zip file)	Table 2/Table 2.pdf

Statistical analyses

Statistical analysis title	Gold microparticle delivery
Comparison groups	One arm v Gold microparticle analyses
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the participatns during the study period

Adverse event reporting additional description:

AEs were mostly erythema and scaling. Patients were advised to pause A-BPO for up to two days or apply the gel once every other day for a 4-5 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	6

Reporting groups

Reporting group title	Patients

Reporting group description: -

Serious adverse events	Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 15 (53.33%)		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	8 / 15 (53.33%)		
occurrences (all)	8		
Dryness			
subjects affected / exposed	8 / 15 (53.33%)		
occurrences (all)	8		

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.

Limitations of the study included the uncontrolled design, the limited sample size, and only 6-weeks treatment with A-BPO.

Notes: