Clinical trial results:
Topical brimonidine reduces IPL-induced erythema without affecting efficacy: a randomized controlled trial in patients with facial telangiectasias

Summary

EudraCT number	2015-004789-27
Trial protocol	DK
Global end of trial date	13 January 2017

Results information

Result version number	v1 (current)
This version publication date	19 January 2018
First version publication date	19 January 2018
Summary attachment (see zip file)	Abstract (ABSTRACT.pdf)

Trial information

Trial identification

Sponsor protocol code	21.November.2015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02761174
WHO universal trial number (UTN)	-
Other trial identifiers	H-15018114: ID-number: 16/8/76

Notes:

Sponsors

Sponsor organisation name	Bispebjerg Hospital
Sponsor organisation address	Bispebjerg bakke 23, København NV, Denmark, 2400
Public contact	Dermatologisk Afdeling, Bispebjerg Hospital, 0045 20736670, acvissing@gmail.com
Scientific contact	Dermatologisk Afdeling, Bispebjerg Hospital, 0045 20736670, acvissing@gmail.com

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	29 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 January 2017
Global end of trial reached?	Yes
Global end of trial date	13 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We aimed at investigating, whether topical brimonidine could reduce IPL- induced post-inflammatory response in terms of erythema, oedema and pain in patients with facial telangiectasias.

Protection of trial subjects:

Treatments were performed by highly trained dermatologist and study assistants applied brimonidine at the hospital, where patients were observed for more than 30 minutes after.

Background therapy:

Same procedure followed after each of 3 facial Intense Pulsed Light (IPL) treatments, given at 3-week intervals. Patients received IPL to both sides of the face (allocated side and control side) using PR applicator with wavelength bands of 530-750 nm and spot size 10x48 mm. Colourless gel was applied before IPL on treatment areas to optimize optical coupling between the light guide and the skin. Similar IPL-settings were applied between facial sides to induce equal immediate IPL-responses guided by clinical endpoints of erythema, vasoconstriction or transient purpura.

Evidence for comparator: -

Actual start date of recruitment	14 March 2016
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: 10
Country: Number of subjects enrolled	Belgium: 9
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	17
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Inclusion criteria were patients with symmetrical distribution of moderate to severe facial telangiectasias, based on clinical photo-guidelines. Males and females at 18-65 years old with Fitzpatrick skin types I-III were included.

Pre-assignment

Screening details:

Inclusion criteria were patients with symmetrical distribution of moderate to severe facial telangiectasias, based on clinical photo-guidelines. Males and females at 18-65 years old with Fitzpatrick skin types I-III were included. All fertile women documented non-reactive urine pregnancy test at the day of inclusion and used effective birth control

Pre-assignment period milestones

Number of subjects started	19
Intermediate milestone: Number of subjects	baseline, 1. treatment: 19
Intermediate milestone: Number of subjects	the day after baseline: 19
Intermediate milestone: Number of subjects	2. treatment: 19
Intermediate milestone: Number of subjects	3. treatment: 19
Intermediate milestone: Number of subjects	final follow-up: 19
Number of subjects completed	19

Period 1

Period 1 title	Baseline to follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Data analyst, Assessor[2]

Blinding implementation details:

Randomization was conducted with consecutively numbered, closed, non-transparent envelopes containing a computer-generated allocation. Envelopes were opened in a numeric order immediately before first treatment. The envelope contained either the letter L (left) or R (right), indicating the facial side receiving topical brimonidine.

Arms

Arm title	Brimonidine and air-cooling (treatment) vs air-cooling alone

Arm description:

The trial was a split-face trial, thus patients were their own control in which one side of the face received topical brimonidine and air-cooling and the other side air-cooling alone (control)

Arm type	Experimental
Investigational medicinal product name	Brimonidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

pea sized amount

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: Evaluator and data analyst was blinded to treatment, while patients and study assistants that applied brimonidine were not

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Evaluator and data analyst was blinded to treatment, while patients and study assistants that applied brimonidine were not

Number of subjects in period 1	Brimonidine and air-cooling (treatment) vs air-cooling alone
Started	19
baseline, 1. treatment	19
The day after the first treatment	19
2. treatment, 3-weeks after baseline	19
3. treatment, 6 weeks after baseline	19
Follow-up, 10 weeks after baseline	19
Completed	19

Baseline characteristics

Reporting groups

Reporting group title	Baseline to follow-up

Reporting group description: -

Reporting group values	Baseline to follow-up	Total	
Number of subjects	19	19	
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)	17	17	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	13	13	
Male	6	6	

Subject analysis sets

Subject analysis set title	brimonidine and air-cooling vs. air-cooling alone
Subject analysis set type	Full analysis

Subject analysis set description:

NOTE!! This was an intra-individual split-face trial, where patients were their own control. Therefor NOT 38 patients BUT in total 19 patients were included in full analysis

Reporting group values	brimonidine and air-cooling vs. air-cooling alone		
Number of subjects	19		
Age categorical 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)	17		
From 65-84 years	2		
85 years and over	0		

Gender categorical Units: Subjects			
Female	13		
Male	6		

End points

End points reporting groups

Reporting group title	Brimonidine and air-cooling (treatment) vs air-cooling alone

Reporting group description:

The trial was a split-face trial, thus patients were their own control in which one side of the face received topical brimonidine and air-cooling and the other side air-cooling alone (control)

Subject analysis set title	brimonidine and air-cooling vs. air-cooling alone
Subject analysis set type	Full analysis

Subject analysis set description:

NOTE!! This was an intra-individual split-face trial, where patients were their own control. Therefor NOT 38 patients BUT in total 19 patients were included in full analysis

Primary: clinical on-site evaluation of erythema and oedema

End point title	clinical on-site evaluation of erythema and oedema

End point description:

Blinded clinical on-site evaluation of erythema and oedema were assessed separately on a validated 5-point scale and 4-point scale, respectively by the same blinded-evaluators at each site

End point type	Primary

End point timeframe:

primary outcomes were evaluated separately for brimonidine and control side immediately after each of the 3 IPL-treatment and at 30-60 minutes after incubation of brimonidine and were further evaluated the day after the first treatment and at follow-up

End point values	Brimonidine and air-cooling (treatment) vs air-cooling alone	brimonidine and air-cooling vs. air-cooling alone		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	19	19		
Units: 0-4, 0-3	19	19		

Attachments (see zip file)	summary/ABSTRACT.pdf

Statistical analyses

Statistical analysis title	non-parametric Wilcoxon signed rank test

Statistical analysis description:

Brimonidine and air-cooling was compared to air-cooling alone, in this split-face intra-individual study where patients were there own control

Comparison groups	Brimonidine and air-cooling (treatment) vs air-cooling alone v brimonidine and air-cooling vs. air-cooling alone

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Wilcoxon signed rank test
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided

Notes:

[1] - non-parametric Wilcoxon signed rank test

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

During the whole study

Adverse event reporting additional description:

No adverse events directly attributable to topical brimonidine were observed during trial period. IPL-treatment induced superficial wounds after application of fluences higher than median levels in three patients on both brimonidine and control sides that resolved before follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	superficial wounds
Dictionary version	1

Reporting groups

Reporting group title	patients

Reporting group description: -

Serious adverse events	patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse events directly attributable to topical brimonidine were observed during trial period. IPL-treatment induced superficial wounds after application of fluences higher than median levels in three patients on both brimonidine and control sides that resolved before follow-up.

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

None reported