Clinical trial results:
Epidermal Nerve Fibre Density Reduction as a Function of Application Time of topical high-dose and low-dose Capsaicin

Summary

EudraCT number	2012-002406-46
Trial protocol	AT
Global end of trial date	03 April 2020

Results information

Result version number	v1 (current)
This version publication date	02 June 2020
First version publication date	02 June 2020
Summary attachment (see zip file)	Summary Capsaicin (CAPSAICIN_ich-e-3-structure-synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	08.10.2012

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Dept. of Anaesthesia, Intensive Care and Pain Management, Medical University Vienna, 0043 1404004108, joerg.hiesmayr@meduniwien.ac.at
Scientific contact	Dept. of Anaesthesia, Intensive Care and Pain Management, Medical University Vienna, 0043 1404004108, joerg.hiesmayr@meduniwien.ac.at

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	27 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2013
Global end of trial reached?	Yes
Global end of trial date	03 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Comparison of the effect of increasing application time of different Capsaicin doses on the density of epidermal nerve fibres

Protection of trial subjects:

If the application of the capsaicin patch on the skin was painful for the study participants, the volunteers could request pain-killers on demand.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2012
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	Austria: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place from August 2012 till October 2012. The healthy volunteers where recruited by notices at the black boards at the Medical University Vienna. Participants were mainly recruited from medical students.

Pre-assignment

Screening details:

Only healthy volunteers were included. During the screening visit participants where evaluated regarding their over all health and in particular a neurological status was assessed. Only non-pregnant women were included. Pregnancy tests were conducted prior to inclusion.
Twelve subject where screened and all could be included.

Period 1

Period 1 title	Capsaicin Application (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

randomised, placebo-controlled, observer-blinded trail

Arms

Are arms mutually exclusive?	No
Arm title	Capsaicin 0,05 %

Arm description:

Each participant got capsaicin 0,05% ointment (active comparator) on the one thigh

Arm type	Active comparator
Investigational medicinal product name	Capsaicin 0,05%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

Capsaicin 0,05% ointment was administered to five pre-defined areas (size 3x3cm) on one thigh - a sixth area remained untreated as reference area.
After certain points of time, one blob of ointment after the other was removed consecutively in a randomised manner.
One week and five weeks after the application, one skin punch biospy was taken of every application area and the epidermal nerve fibre density was analysed.

Arm title	Capsaicin 8%

Arm description:

Each participant got capsaicin 8% patch (active comparator) on the other thigh

Arm type	Experimental
Investigational medicinal product name	Qutenza
Investigational medicinal product code	EU/1/09/524/001
Other name	Capsaicin 8% patch
Pharmaceutical forms	Transdermal patch
Routes of administration	Transdermal use

Dosage and administration details:

Pieces (size 3x3cm) of a Capsaicin 8% patch were administered to five pre-defined areas on one thigh - a sixth area remained untreated as reference area.
After certain points of time, one patch after the other was removed consecutively in a randomised

manner.
One week and five weeks after the application, one skin punch biospy was taken of every application area and the epidermal nerve fibre density was analysed.

Notes:

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

Justification: randomised, placebo-controlled, observer-blinded trail

Number of subjects in period 1	Capsaicin 0,05 %	Capsaicin 8%
Started	12	12
Skin biopsy week 1	12	12
Skin biopsy week 5	12	12
Capsaicin application	12	12
Completed	12	12

Baseline characteristics

Reporting groups	
Reporting group title	Capsaicin 0,05 %
Reporting group description:	
Each participant got capsaicin 0,05% ointment (active comparator) on the one thigh	
Reporting group title	Capsaicin 8%
Reporting group description:	
Each participant got capsaicin 8% patch (active comparator) on the other thigh	

Reporting group values	Capsaicin 0,05 %	Capsaicin 8%	Total
Number of subjects	12	12	12
Age categorical			
Healthy adult volunteers aged 18-64 years where included			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	12	12
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	6	6	6
Male	6	6	6

End points

End points reporting groups

Reporting group title	Capsaicin 0,05 %
Reporting group description:	
Each participant got capsaicin 0,05% ointment (active comparator) on the one thigh	
Reporting group title	Capsaicin 8%
Reporting group description:	
Each participant got capsaicin 8% patch (active comparator) on the other thigh	

Primary: Change in epidermal nerve fibre density without capsaicin treatment and one week after capsaicin treatment

End point title	Change in epidermal nerve fibre density without capsaicin treatment and one week after capsaicin treatment
End point description:	
End point type	Primary
End point timeframe:	
Epidermal nerve fibre density one week after the capsaicin treatment	

End point values	Capsaicin 0,05 %	Capsaicin 8%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: 0,1				
arithmetic mean (standard deviation)	15.2 (± 7.4)	11.9 (± 7.8)		

Statistical analyses

Statistical analysis title	ANOVA
Statistical analysis description:	
Analysis was performed with an ANOVA for Latin squares, in the course of a Randomised Block Factorial Design, whereas the different capsaicin dosages and application durations are specified as inner-block factors. For analysis of the impact of gender this ANOVA was extended to a Split-Plot Design. For recognition of discordant values or skewness of distribution, testing of the residues was preceded to all statistical analysis.	
Comparison groups	Capsaicin 0,05 % v Capsaicin 8%
Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)

Variability estimate	Standard deviation

Secondary: Change in epidermal nerve fibre density without capsaicin treatment and five weeks after capsaicin treatment

End point title	Change in epidermal nerve fibre density without capsaicin treatment and five weeks after capsaicin treatment

End point description:

End point type	Secondary

End point timeframe:

Epidermal nerve fibre density five weeks after capsaicin treatment

End point values	Capsaicin 0,05 %	Capsaicin 8%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: 0,1				
arithmetic mean (standard deviation)	16.1 (± 6.2)	14.8 (± 6.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Study period	
Adverse event reporting additional description:	
daily questionnaire; volunteers hab to indicate pain, swelling, rubor at the capsaicin application sites on the skin	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Capsaicin 0,05 %
Reporting group description:	
Each participant got capsaicin 0,05% ointment (active comparator) on the one thigh	
Reporting group title	Capsaicin 8%
Reporting group description:	
Each participant got capsaicin 8% patch (active comparator) on the other thigh	

Serious adverse events	Capsaicin 0,05 %	Capsaicin 8%	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Capsaicin 0,05 %	Capsaicin 8%	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 12 (66.67%)	5 / 12 (41.67%)	
Skin and subcutaneous tissue disorders			
Pain of skin	Additional description: some participants indicated capsaicin related application pain - with a maximum pain level of 2 on the visual analog scale from 0-10 (no pain - maximum pain)		
subjects affected / exposed	8 / 12 (66.67%)	5 / 12 (41.67%)	
occurrences (all)	8	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 October 2012	In addition the to evaluation of the density of epidermal nerve fibers one week after the capsaicin application, the amendment was introduced to be able to evaluate the epidermal nerve fibres five weeks after the capsaicin application.

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.

the number of participants of twelve was small

Notes: