Clinical trial results:
The role of pre-emptive analgesia with Qutenza (topical capsaicin 8%) in preventing neuropathic pain following lower limb amputation: a pilot randomised controlled study

Summary

EudraCT number	2012-001587-30
Trial protocol	GB
Global end of trial date	12 April 2017

Results information

Result version number	v1 (current)
This version publication date	19 January 2020
First version publication date	19 January 2020

Trial information

Trial identification

Sponsor protocol code	GU11SU387

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01748435
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow and Clyde
Sponsor organisation address	Dalnair Street, Glagsow, United Kingdom,
Public contact	Maureen Travers, NHS Greater Glasgow and Clyde, 44 01412116389, Maureen.Travers@ggc.scot.nhs.uk
Scientific contact	Maureen Travers, NHS Greater Glasgow and Clyde, 44 01412116389, Maureen.Travers@ggc.scot.nhs.uk

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	Interim
Date of interim/final analysis	12 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 April 2017
Global end of trial reached?	Yes
Global end of trial date	12 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Does the pre-operative application of topical Qutenza (capsaicin 8%)to patients undergoing amputation reduce chronic nerve pain at 12 weeks post-operatively?

Protection of trial subjects:

Patients all underwent verbal and written consent.
All patients were treated whilst inpatients in the Vascular ward at either Queen Elizabeth University Hospital or Western Infirmary, Glasgow. Regular review by study team day 1,3,7 post-application of the drug and review of the treatment site. Single application of the drug.
Small research team were aware of safety of all research participants throughout the trial.
Patients were given a Patient Alert Card to permit identification as a trial participant if required.
SAE reporting in place and unblinding procedure in the event of serious reaction.
Safety precautions and protocol for administration of the study drug/placebo and training of the research team in safe application of the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2014
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	United Kingdom: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	8
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the Department of Vascular Surgery at the Western Infirmary and Queen Elizabeth University Hospitals, Glasgow between 25th June 2014 and 11th January 2017. Potential participants were identified by a member of the clinical or research team and a verbal referral made. 30 patients were recruited.

Pre-assignment

Screening details:

40 patients were screened for participation. 8 were excluded as the did not meet inclusion criteria- unable to provide consent (2), surgery planned <24 hours from screening visit (2), traumatic amputation (1), open wound at site of intended treatment (1). 2 patients declined to participate.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

A single treatment was required for each patient in the study. The patient was blinded by applying a sheet across the treatment area.
Placebo patch and gel-Tegaderm/ Aquagel used as placebo and the application process was repeated identically for both treatment arms.
Clinical team were unaware of the treatment allocation.
Unblinding envelopes were held and patients given Patient Alert Cards in case need for unblinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment

Arm description:

Single application of Qutenza

Arm type	Experimental
Investigational medicinal product name	Qutenza (topical capsaicin 8%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal solution
Routes of administration	Transdermal use

Dosage and administration details:

Each 280cm2 Qutenza® patch contains 179mg of capsaicin. Patients could be treated with a maximum of 4 patches (716g of capsaicin)/control patches. The exact dose administered was determined by the size of the area to be treated.

Arm title	Control

Arm description:

Single application of placebo (Tegaderm) patch

Arm type	Placebo
Investigational medicinal product name	Tegaderm
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous patch
Routes of administration	Cutaneous use

Dosage and administration details:

Single application. As required to replicate Qutenza treatment

Number of subjects in period 1	Treatment	Control
Started	15	15
Completed	12	15
Not completed	3	0
Adverse event, serious fatal	1	-
Consent withdrawn by subject	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment
Reporting group description:	
Single application of Qutenza	
Reporting group title	Control
Reporting group description:	
Single application of placebo (Tegaderm) patch	

Reporting group values	Treatment	Control	Total
Number of subjects	15	15	30
Age categorical 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)	6	2	8
From 65-84 years	9	13	22
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	8	13
Male	10	7	17

Subject analysis sets	
Subject analysis set title	Treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Qutenza treatment	
Subject analysis set title	Control
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Placebo control	

Reporting group values	Treatment	Control	
Number of subjects	15	15	
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)	5	2	
From 65-84 years	9	13	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	8	
Male	9	7	

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: Single application of Qutenza	
Reporting group title	Control
Reporting group description: Single application of placebo (Tegaderm) patch	
Subject analysis set title	Treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description: Qutenza treatment	
Subject analysis set title	Control
Subject analysis set type	Intention-to-treat
Subject analysis set description: Placebo control	

Primary: Pain score (VAS) 12 weeks

End point title	Pain score (VAS) 12 weeks
End point description: Patient reported visual analogue pain score at 12 weeks	
End point type	Primary
End point timeframe: 12 weeks	

End point values	Treatment	Control	Treatment	Control
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	15	14	15
Units: VAS (0-10)				
arithmetic mean (inter-quartile range (Q1-Q3))	5 (4 to 8)	4 (4 to 7)	5 (4 to 8)	4 (4 to 7)

Statistical analyses

Statistical analysis title	Visual analysis score- difference between groups
Statistical analysis description: Median VAS was compared between Qutenza and Controls groups at baseline, and post treatment- days 1 and 7 , and weeks 6 and 12	
Comparison groups	Treatment v Control

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Chi-squared

Notes:

[1] - This was a small pilot study with VAS as primary outcome measure, and median difference between groups at different time points assessed. Secondary outcome measures were treated similarly.

Secondary: Assessment of treated area

End point title	Assessment of treated area

End point description:

Assessment of treated area day 0

End point type	Secondary

End point timeframe:

Day 0

End point values	Treatment	Control	Treatment	Control
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	15	11	15
Units: Assessment of skin				
No erythema	11	15	11	15
Mild erythema	0	0	0	0
Extensive erythema	0	0	0	0
Mild blistering	0	0	0	0
Severe blistering	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Pain score (VAS) day 7

End point title	Pain score (VAS) day 7

End point description:

End point type	Secondary

End point timeframe:

Day 7

End point values	Treatment	Control	Treatment	Control
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	13	15	13	15
Units: VAS pain score				
median (inter-quartile range (Q1-Q3))	6 (4 to 8)	7 (5 to 7)	6 (4 to 8)	7 (5 to 7)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were reporting within 24 hours

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Treatment (Qutenza)
Reporting group description: -	
Reporting group title	Control (placebo)

Reporting group description: -

Serious adverse events	Treatment (Qutenza)	Control (placebo)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Death	Additional description: Death from critical limb ischaemia		
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Revision amputation	Additional description: Need to revise amputation from BKA to AKA		
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Upper GI bleed	Additional description: Self-resolving upper GI bleed		
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment (Qutenza)	Control (placebo)	
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 15 (26.67%)	1 / 15 (6.67%)	
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Mild erythema following removal of the patch was reported in 5 patients (4 in the treatment arm and 1 in the control arm). By the day of surgery, one patient in the treatment arm still had mild erythema. Otherwise there were no significant skin react		
alternative assessment type: Non-systematic subjects affected / exposed	4 / 15 (26.67%)	1 / 15 (6.67%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2015	Change of CI/PI from Emma Aitken to David Kingsmore due to relocation.

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.

This was a small pilot study. Qutenza safe in this patient cohort but no benefit in pain scores demonstrated. Logistically difficult to undertake in emergent patients. Lack of blinding of study team potential source of bias.

Notes: