Clinical trial results:
A phase II RCT of topical menthol gel versus placebo in the treatment of chemotherapy induced peripheral neuropathic pain

Summary

EudraCT number	2013-003968-31
Trial protocol	GB
Global end of trial date	06 October 2022

Results information

Result version number	v1 (current)
This version publication date	10 June 2023
First version publication date	10 June 2023

Trial information

Trial identification

Sponsor protocol code	AC15006

Additional study identifiers

ISRCTN number	ISRCTN69917256
ClinicalTrials.gov id (NCT number)	NCT04276727
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ACCORD
Sponsor organisation address	QMRI, 47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
Public contact	Prof Marie Fallon, University of Edinburgh, +44 1316518611, marie.fallon@ed.ac.uk
Scientific contact	Prof Marie Fallon, University of Edinburgh, +44 1316518611, marie.fallon@ed.ac.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	Final
Date of interim/final analysis	06 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2022
Global end of trial reached?	Yes
Global end of trial date	06 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether 6 weeks of topical 3% menthol gel provides effective analgesia for neuropathic pain, using the Brief Pain Inventory Short Form to assess this outcome.

Protection of trial subjects:

No issues

Background therapy:

No issues

Evidence for comparator:

No issues

Actual start date of recruitment	04 November 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	United Kingdom: 52
Worldwide total number of subjects	52
EEA total number of subjects	0

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)	30
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

52 participants recruited - 27 in menthol gel arm and 25 in placebo

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	52
Number of subjects completed	52

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	menthol gel

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	5% menthol gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

As per protocol

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

As per protocol

Number of subjects in period 1	menthol gel	Placebo
Started	27	25
Completed	27	25

Period 2	
Period 2 title	Week 6
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	menthol gel
Arm description: Patients on active IMP	
Arm type	Active comparator
Investigational medicinal product name	5% menthol gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical
Dosage and administration details: As per protocol	
Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical
Dosage and administration details: As per protocol	

Number of subjects in period 2	menthol gel	Placebo
Started	27	25
Completed	26	23
Not completed	1	2
Consent withdrawn by subject	1	1
Physician decision	-	1

Baseline characteristics

End points

End points reporting groups	
Reporting group title	menthol gel
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	menthol gel
Reporting group description: Patients on active IMP	
Reporting group title	Placebo
Reporting group description: -	

Primary: A clinically significant reduction in pain (at least a 30% decrease in total BPI SF score as relates to the index neuropathic pain) between baseline and 6 weeks

End point title	A clinically significant reduction in pain (at least a 30% decrease in total BPI SF score as relates to the index neuropathic pain) between baseline and 6 weeks

End point description:

A clinically significant reduction in pain (at least a 30% decrease in total BPI SF score as relates to the index neuropathic pain) between baseline and 6 weeks

End point type	Primary

End point timeframe:

6 weeks

End point values	menthol gel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	23		
Units: people	12	10		

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	menthol gel v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.851
Method	Binomial
Parameter estimate	Risk difference (RD)
Point estimate	-2.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.56
upper limit	25.21

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 hours

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Menthol Gel Group
Reporting group description: -	
Reporting group title	Placebo Group

Reporting group description: -

Serious adverse events	Menthol Gel Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 27 (3.70%)	2 / 25 (8.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Eye disorders			
Retinal detachment	Additional description: Unrelated to trial		
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Perforated bowel	Additional description: Admitted for emergency surgery. Unrelated to trial		
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Upper respiratory tract infection	Additional description: Unrelated to trial		
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Menthol Gel Group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 27 (48.15%)	9 / 25 (36.00%)	
Injury, poisoning and procedural complications			
Injury	Additional description: Minor injuries (burn, blisters, being hit by an object) - unrelated to study		
subjects affected / exposed	1 / 27 (3.70%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Anaemia	Additional description: Unrelated to study		
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Sleep disorder	Additional description: Unrelated		
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Hernia	Additional description: Unrelated to study		
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Diarrhoea	Additional description: Unrelated to study		
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Itch	Additional description: Itch/redness/dry skin - possibly related		
subjects affected / exposed	4 / 27 (14.81%)	2 / 25 (8.00%)	
occurrences (all)	5	2	
Musculoskeletal and connective tissue disorders			
Falls	Additional description: Unrelated to study		
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Pain	Additional description: non-specific chest, arthritic, cramp - all unrelated to study		
subjects affected / exposed	0 / 27 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Back pain	Additional description: unrelated		
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)	
occurrences (all)	2	0	

Infections and infestations			
urinary tract infections	Additional description: Unrelated to study		
subjects affected / exposed	2 / 27 (7.41%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Respiratory tract infection	Additional description: Unrelated to study		
subjects affected / exposed	5 / 27 (18.52%)	1 / 25 (4.00%)	
occurrences (all)	5	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 October 2019	SA.04
25 February 2020	SA.05
18 October 2021	SA.06

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 March 2020	Trial halted to new recruitment due to COVID pandemic. Patients already recruited continued as per protocol. Permission to restart recruitment was granted on 17 August 2020.	17 August 2020

Notes:

Limitations and caveats

None reported