Clinical trial results:
A double blind, placebo controlled, randomised dose escalation trial to investigate the safety and efficacy of topical salbutamol in the improvement of scar appearance when applied to approximated wound margins in healthy volunteers.

Short title: A trial to assess the safety and efficacy of topical salbutamol in healthy volunteers

Summary

EudraCT number	2017-003118-15
Trial protocol	GB
Global end of trial date	01 July 2019

Results information

Result version number	v1 (current)
This version publication date	06 January 2021
First version publication date	06 January 2021

Trial information

Trial identification

Sponsor protocol code	97807

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University Hospitals of Leicester - NHS Trust
Sponsor organisation address	Leicester Royal Infirmary, Infirmary Square, Leicester, United Kingdom, LE1 5WW
Public contact	David Fairlamb, ProTherax Ltd, +44 1274561815, davidfairlamb@protherax.com
Scientific contact	David Fairlamb, ProTherax Ltd, +44 1274561815, davidfairlamb@protherax.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	23 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2019
Global end of trial reached?	Yes
Global end of trial date	01 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the safety and tolerance of topically applied salbutamol gel, when applied topically to the approximated wound margins of male and female subjects following surgical incisions.

Protection of trial subjects:

Trial subjects were recruited sequentially is escalating dose groups, and escalation of salbutamol concentrations (2.5mM, 5.0mM, and 10.0mM) was based on an assessment by an independent Data Safety Monitoring Committee (DSMC) which assessed safety of the IMP after the last patient of each group had reached Day 14

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2017
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: 45
Worldwide total number of subjects	45
EEA total number of subjects	45

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)	45

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects recruited to the study were healthy volunteers, recruited between Jan 2018 and 01 July 2018. Last subject competed follow-up in 01 July 2019. All subjects were recruited in the UK.

Pre-assignment

Screening details:

Healthy volunteers aged 18-50, who provided written informed consent, registered on The Over Volunteering Prevention System (TOPS), had a BMI of 15.0-35.0 kg/m2 and who had acceptable clinical laboratory tests. Total number of subjects screened was 51.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

This study was a double-blind trial using a placebo (vehicle) gel without salbutamol as the comparator. There was no visual, tactile or odour differences between the two gel products. All subjects, investigators and staff involved in trial related assessments were blinded to study treatment administered to each incision site.

Arms

Are arms mutually exclusive?	Yes
Arm title	Salbutamol Gel 2.5mM vs placebo

Arm description:

Within patient study, in which an incision on one arm was dosed with Salbutamol Gel 2.5mM and one arm was dosed with placebo.

Arm type	IMP vs Placebo
Investigational medicinal product name	Salbutamol Gel 2.5mM
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

1mL administered to the incisional wound site every day for 60 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

1mL administered to the incisional wound site daily for 60 days

Arm title	Salbutamol Gel 5.0mM vs Placebo

Arm description:

Within subject comparison of salbutamol Gel 5.0mM administered to a wound on one arm compared with Placebo Gel administered to the contralateral arm

Arm type	IMP vs Placebo

Investigational medicinal product name	Salbutamol Gel 5.0mM
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

1mL administered to the incisional wound site daily for 60 days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

1mL administered to the incisional wound site daily for 60 days

Arm title	Salbutamol Gel 10mM vs placebo

Arm description:

Within subject comparison in which Salbutamol Gel 10mM was administered to one arm and placebo gel to the contralateral arm

Arm type	IMP vs Placebo
Investigational medicinal product name	Salbutamol 10mM Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

1mL administered to the incisional wound site daily for 60 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

1mL administered to the incisional wound site daily for 60 days

Number of subjects in period 1	Salbutamol Gel 2.5mM vs placebo	Salbutamol Gel 5.0mM vs Placebo	Salbutamol Gel 10mM vs placebo
Started	15	15	15
Completed	15	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Salbutamol Gel 2.5mM vs placebo
Reporting group description:	
Within patient study, in which an incision on one arm was dosed with Salbutamol Gel 2.5mM and one arm was dosed with placebo.	
Reporting group title	Salbutamol Gel 5.0mM vs Placebo
Reporting group description:	
Within subject comparison of salbutamol Gel 5.0mM administered to a wound on one arm compared with Placebo Gel administered to the contralateral arm	
Reporting group title	Salbutamol Gel 10mM vs placebo
Reporting group description:	
Within subject comparison in which Salbutamol Gel 10mM was administered to one arm and placebo gel to the contralateral arm	

Reporting group values	Salbutamol Gel 2.5mM vs placebo	Salbutamol Gel 5.0mM vs Placebo	Salbutamol Gel 10mM vs placebo
Number of subjects	15	15	15
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Subject Age			
Units: years arithmetic mean standard deviation	 21.7 ± 2.6	 22.6 ± 2.2	 27.2 ± 8.3
Gender categorical Units: Subjects			
Female	7	6	10
Male	8	9	5
Fitzpatrick Skin Scale			
Fitzpatrick skin type of subjects			
Units: Subjects			
I-	6	8	4
II-	8	5	8
III-IV	1	0	1
V-VI	0	2	2

Reporting group values	Total		
Number of subjects	45		

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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Subject Age			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	23		
Male	22		
Fitzpatrick Skin Scale			
Fitzpatrick skin type of subjects			
Units: Subjects			
I-	18		
II-	21		
III-IV	2		
V-VI	4		

End points

End points reporting groups

Reporting group title	Salbutamol Gel 2.5mM vs placebo
Reporting group description:	
Within patient study, in which an incision on one arm was dosed with Salbutamol Gel 2.5mM and one arm was dosed with placebo.	
Reporting group title	Salbutamol Gel 5.0mM vs Placebo
Reporting group description:	
Within subject comparison of salbutamol Gel 5.0mM administered to a wound on one arm compared with Placebo Gel administered to the contralateral arm	
Reporting group title	Salbutamol Gel 10mM vs placebo
Reporting group description:	
Within subject comparison in which Salbutamol Gel 10mM was administered to one arm and placebo gel to the contralateral arm	

Primary: Proportion of patients achieving salbutamol PK <30mg/mL

End point title	Proportion of patients achieving salbutamol PK <30mg/mL[1]
End point description:	
Pharmacokinetic analysis was summarised for each time of the sample time points. These data were used to calculate the Cmax, Tmax, T1/2 and AUC24 hours for the cutaneous route of administration. The proportion of individuals with Salbutamol peak plasma concentration less than 30ng/ml for the 24 hours following gel application at day 0 were also summarised for each dose	
End point type	Primary
End point timeframe:	
Day 0	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As a pilot safety study, the number and percentage of participants in each dose group with the primary outcome (i.e. Salbutamol peak plasma concentration in the 24 hours following gel administration at day 0 greater than 30ng/ml), are presented but no statistical tests were performed.

End point values	Salbutamol Gel 2.5mM vs placebo	Salbutamol Gel 5.0mM vs Placebo	Salbutamol Gel 10mM vs placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Subjects	15	15	15	

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of patients achieving salbutamol PK <30mg/mL

End point title	Proportion of patients achieving salbutamol PK <30mg/mL[2]
End point description:	
End point type	Primary

End point timeframe:

Day 10- to 11

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As a pilot safety study, the number and percentage of participants in each dose group with the primary outcome (i.e. Salbutamol peak plasma concentration in the 24 hours following gel administration at day 0 greater than 30ng/ml), are presented but no statistical tests were performed.

End point values	Salbutamol Gel 2.5mM vs placebo	Salbutamol Gel 5.0mM vs Placebo	Salbutamol Gel 10mM vs placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	15	15	
Units: Subjects	13	15	15	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 Months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	Salbutamol Gel 2.5mM vs placebo
Reporting group description:	
Within patient study, in which an incision on one arm was dosed with Salbutamol Gel 2.5mM and one arm was dosed with placebo.	
Reporting group title	Salbutamol Gel 5.0mM vs Placebo
Reporting group description:	
Within subject comparison of salbutamol Gel 5.0mM administered to a wound on one arm compared with Placebo Gel administered to the contralateral arm	
Reporting group title	Salbutamol Gel 10mM vs placebo
Reporting group description:	
Within subject comparison in which Salbutamol Gel 10mM was administered to one arm and placebo gel to the contralateral arm	

Serious adverse events	Salbutamol Gel 2.5mM vs placebo	Salbutamol Gel 5.0mM vs Placebo	Salbutamol Gel 10mM vs placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Salbutamol Gel 2.5mM vs placebo	Salbutamol Gel 5.0mM vs Placebo	Salbutamol Gel 10mM vs placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)	6 / 15 (40.00%)	10 / 15 (66.67%)
Injury, poisoning and procedural complications			

Blister			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Ankle fracture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Neurogenic shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Syncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Tooth impacted			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			

Polycystic ovaries			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Dermatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Foot fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
Infected bite			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Viral rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bacterial vaginosis			

subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

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