



Clinical trial results:

A Phase IV, Randomised, Double-Blind, Controlled, Parallel Group Trial to Evaluate the Effectiveness and Safety of Balneum Plus vs Emollient in the Treatment of Uraemic Pruritus in Haemodialysis Patients.

Summary

EudraCT number	2014-005594-36
Trial protocol	GB
Global end of trial date	26 December 2017

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	PHT/2014/107
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Additional study identifiers

ISRCTN number	ISRCTN13971661
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Portsmouth Hospitals NHS Trust
Sponsor organisation address	Queen Alexandra Hospital, Cosham, Portsmouth, United Kingdom, PO6 3LY
Public contact	Jacqueline Nevols, Portsmouth Hospitals NHS Trust, +44 02392286000, jacqueline.nevols@porthosp.nhs.uk
Scientific contact	Jacqueline Nevols, Portsmouth Hospitals NHS Trust, +44 02392286000, jacqueline.nevols@porthosp.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	Final
Date of interim/final analysis	26 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 December 2017
Global end of trial reached?	Yes
Global end of trial date	26 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare itch intensity as measured by a Visual Analogue Scale after 4 weeks treatment with Balneum Plus cream vs emollient control in patients with uraemic pruritus.

Protection of trial subjects:

Trial subjects had contact with study staff on a weekly basis - and had contact details to report problems outside of scheduled visits.

Background therapy:

All trial subjects were on maintenance haemodialysis for treatment of end-stage renal disease. Most of the trial subjects were on multiple medications -for example antihypertensives and phosphate binders. All medications were recorded at the time of study entry and subjects were stratified according to antihistamine use.

Evidence for comparator:

For the comparator group - a basic emollient was used (E45). There is no evidence in the literature that simple emollients (without active ingredients) improve the symptoms of uraemic pruritus.

Actual start date of recruitment	04 January 2016
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: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	27

From 65 to 84 years	28
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from the Wessex Kidney Centre's dialysis units. The research nurse visited each patient to inquire about symptoms of pruritus and their potential willingness to take part in a clinical trial.

Pre-assignment

Screening details:

Potential subjects were screen according to the inclusion and exclusion criteria for the trial by the research nurse at the dialysis centre.

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	Investigator, Monitor, Assessor, Subject

Blinding implementation details:

Randomisation list generated by the study statistician. The list was kept securely in the Trust Pharmacy. Study team (CI and research nurses) had no access to the randomisation list. Upon successful recruitment of a trial subject - the patient was randomised and prescribed the trial cream. Both the study cream and comparator looked identical and were dispensed in identical containers.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment arm

Arm description:

Balneum Plus - to be applied topically twice daily.

Arm type	Experimental
Investigational medicinal product name	Balneum Plus
Investigational medicinal product code	PL33016/0010
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

The cream was to be applied to affected areas of skin, topically, twice daily, for four weeks.

Arm title	Comparator arm
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Arm description:

E45 cream was used as base cream/control cream

Arm type	Placebo
Investigational medicinal product name	E45
Investigational medicinal product code	PL00063/0404
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

To be applied to affected areas of skin, topically, twice daily, for four weeks.

Number of subjects in period 1	Treatment arm	Comparator arm
Started	29	29
Completed	26	26
Not completed	3	3
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	2
Not complete the course of treatment	1	-
Received transplant, no longer eligible	1	-

Baseline characteristics

Reporting groups

Reporting group title	Treatment arm
Reporting group description: Balneum Plus - to be applied topically twice daily.	
Reporting group title	Comparator arm
Reporting group description: E45 cream was used as base cream/control cream	

Reporting group values	Treatment arm	Comparator arm	Total
Number of subjects	29	29	58
Age categorical			
Adult haemodialysis patients.			
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	15	27
From 65-84 years	17	11	28
85 years and over	0	3	3
Age continuous			
Units: years			
arithmetic mean	64.0	63.4	
standard deviation	± 13.9	± 16.2	-
Gender categorical			
Units: Subjects			
Female	9	9	18
Male	20	20	40
Smoking status			
We documented smoking status as a baseline characteristic.			
Units: Subjects			
Never smoked	11	11	22
Ex-smoker	13	12	25
Current smoker	5	6	11
Cause of End-stage renal disease			
We identified the cause of end-stage renal disease in study participants.			
Units: Subjects			
Glomerulonephritis	9	3	12
Diabetic Nephropathy	3	8	11
Hypertension/renovascular disease	8	4	12
Obstructive Uropathy	2	5	7
Polycystic kidney disease	1	2	3
Other	4	3	7

Unknown	2	4	6
Dialyser size			
We documented the size of dialyser for each participant.			
Units: Subjects			
Small	6	7	13
Medium	11	12	23
Large	12	10	22
Allergic drugs			
Units: Subjects			
No	20	21	41
Yes	9	8	17
Antipruritics			
Units: Subjects			
No	17	17	34
Yes	12	12	24
Emollient use			
Units: Subjects			
No	16	14	30
Yes	13	15	28
Antihistamines use			
Units: Subjects			
No	26	26	52
Yes	3	3	6
Other medication			
Units: Subjects			
No	0	0	0
Yes	29	29	58
Allergies			
Units: Subjects			
No	20	21	41
Yes	9	8	17
Time on Haemodialysis			
Units: Years			
median	1.5	2.6	
inter-quartile range (Q1-Q3)	0.7 to 3.4	0.9 to 4.7	-
C-reactive protein			
Units: milligram(s)/litre			
median	12	10	
inter-quartile range (Q1-Q3)	6 to 20	5 to 19	-
Phosphate Level			
Units: millimole(s)/litre			
arithmetic mean	1.7	1.7	
standard deviation	± 0.6	± 0.6	-
Urea Level			
Units: millimole(s)/litre			
arithmetic mean	18	17	
standard deviation	± 6	± 5	-
Visual Analogue Scale			
Units: Arbitrary Unit			
median	6.5	6.3	
inter-quartile range (Q1-Q3)	4.4 to 8.0	5.1 to 7.3	-

End points

End points reporting groups

Reporting group title	Treatment arm
Reporting group description: Balneum Plus - to be applied topically twice daily.	
Reporting group title	Comparator arm
Reporting group description: E45 cream was used as base cream/control cream	

Primary: Visual Analogue Scale score

End point title	Visual Analogue Scale score
End point description: Patients marked their Itch symptom score on a visual analogue scale.	
End point type	Primary
End point timeframe: VAS score after four weeks treatment.	

End point values	Treatment arm	Comparator arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: cm				
number (not applicable)	2.6	2.0		

Statistical analyses

Statistical analysis title	Visual Analogue Scale at 4 weeks
Statistical analysis description: Primary outcome was compared between groups using ANCOVA. The itch intensity at end of the study was considered as the outcome variable, with the itch intensity at baseline and the use of anti-histamines used as covariates in the analysis. The VAS scores were found to have a positively skewed distribution, and to meet the assumptions of the analysis methods, a log transformation of scores was made, with the analysis performed on the log scale.	
Comparison groups	Treatment arm v Comparator arm
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.64
Method	ANCOVA
Parameter estimate	Adjusted difference ratio
Point estimate	1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.64

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Data on adverse events were collected weekly during the study period and for one week afterwards.

Assessment type	Systematic
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Dictionary used

Dictionary name	Not used
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Dictionary version	0
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Reporting groups

Reporting group title	Balneum Plus
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Reporting group description: -

Reporting group title	Control Emollient
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Reporting group description: -

Serious adverse events	Balneum Plus	Control Emollient	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 29 (13.79%)	3 / 29 (10.34%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Dyspnoea	Additional description: Patient presented at hospital with breathlessness due to previously known heart failure. Patient prescribed bisoprolol and eplerenone and was discharged home later.		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction	Additional description: Patient admitted with Non ST elevation myocardial infarction in a patient with known ischaemic heart disease.		
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure	Additional description: End stage cardiac disease, not fit for further angiography/ intervention. Patient died at home under DNAR order		
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Surgery	Additional description: Patient was treated on Day Case Unit and was admitted overnight. Admitted for formation of left brachio basilic transposition fistula. This was considered routine surgery.		

subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access malfunction	Additional description: Patient admitted with blocked dialysis access. Patient required new tunnelled dialysis line (haemodialysis continues).		
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant	Additional description: Patient admitted for planned transplant surgery. Patient withdrawn from trial as now transplanted and there is an improvement expected in uraemic pruritus. Patient remains in hospital for post surgery monitoring.		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea	Additional description: Patient presented at hospital with diarrhoea as a known clostridium difficile carrier. Patient prescribed oral vancomycin and was considered for faecal transplant, but no longer needed it when symptoms resolved.		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia	Additional description: Patient admitted with shortness of breath and possible pleural effusion. Patient had a chest x-ray		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
urge to urinate & mild hematuria	Additional description: Patient experienced urgency in urinating and passed small amount of blood. Patient referred to urologist for cystoscopy		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Balneum Plus	Control Emollient	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 29 (13.79%)	1 / 29 (3.45%)	
Surgical and medical procedures			
fistuloplasty	Additional description: Planned fistuloplasty		
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Surgery	Additional description: Planned admission for removal of ischaemic finger		
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Inflamed spots	Additional description: Inflamed spots on abdominal skin.		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
itching	Additional description: Itching around cannula site		
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2017	The amendment includes: 1) change of Chief Investigator from Dr Robert Lewis to Dr Jacqueline Nevols, Consultant Nephrologist, who is currently a Co-Investigator and protocol author on the trial; 2) Changes to the study management team due to changes in staffing and their roles; 3) protocol update with the changes from the latest summary of product characteristics for Balneum Plus cream with the safety profile of the drug and expected adverse events; 4) Amended the study inclusion and exclusion criteria to widen the available patient population so that further recruitment is possible; 5) to allow patient questionnaires and case report form to be completed by the patient and returned to the study team by post, with a follow up phone call for any data queries; 6) update to the study questionnaires - a body outline has been replaced by tick boxes for patients to indicate where on the body they are itching in order to make data entry on the study database simpler and more consistent across all patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported