Clinical trial results:
Home Interventions and Light therapy for the treatment of vitiligo

Summary

EudraCT number	2014-003473-42
Trial protocol	GB
Global end of trial date	01 December 2019

Results information

Result version number	v1 (current)
This version publication date	04 January 2020
First version publication date	04 January 2020

Trial information

Trial identification

Sponsor protocol code	14086

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Nottingham
Sponsor organisation address	Lenton Lane, Nottingham, United Kingdom, NG7 2NR
Public contact	University of Nottingham, University of Nottingham, 0115 8467906, angela.shone@nottingham.ac.uk
Scientific contact	University of Nottingham, University of Nottingham, 0115 8467906, angela.shone@nottingham.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	14 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2019
Global end of trial reached?	Yes
Global end of trial date	01 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The priniciple research question is to compare NB-UVB light therapy to a potent topical steroid ointment, to see which treatment is safer and which treatment is more effective in improving the appearance of vitiligo.

PRIMARY OBJECTIVE
To assess the safety and effectiveness of:
- NB-UVB light compared to potent-strength topical corticosteroid
- The combination of NB-UVB light plus topical corticosteroid, compared to topical corticosteroid alone

Protection of trial subjects:

safety data was routinely monitored by the trial team and the DMC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
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: 517
Worldwide total number of subjects	517
EEA total number of subjects	517

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)	71
Adolescents (12-17 years)	48

Adults (18-64 years)	355
From 65 to 84 years	43
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were identified from secondary care, primary care and through local advertising. Randomisation took place in secondary care.

Pre-assignment

Screening details:

Randomisation took place in secondary care hospitals. However, GP practices and other local hospitals in the surrounding area were approached to act as Patient Identification Centres (PICs). GP surgeries sent out invitation letters to patients who may be eligible for the trial. Potential participants were also identified through direct local advert

Pre-assignment period milestones

Number of subjects started	517
Number of subjects completed	517

Period 1

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

Blinding implementation details:

Participants, research nurses, principal investigators and data analysts were blinded to treatment allocation by use of dummy UVB devices and a placebo for TCS. Only the NCTU IT Manager (who creates the treatment allocation schedule), the medical physics staff and NCTU QA staff, responsible for testing and checking the blinding of the devices, will be aware of the allocation of active / placebo treatment. Participants will be randomised by a research nurse via a randomisation website.

Arms

Are arms mutually exclusive?	Yes
Arm title	TCS ointment

Arm description:

topical corticosteroid plus dummy hand-held NB-UVB light

Arm type	Active comparator
Investigational medicinal product name	TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

The total dosage needed by a participant over the course of the 9 month treatment phase is not expected to exceed 270g, and a procedure will be in place to capture any instances where a trial participant has requested more than this amount. Before being prescribed additional ointment, checks will be made to establish the need for additional supplies, and if necessary, a consultation with a dermatologist associated with the trial will be arranged to determine whether or not the participant is using the ointment correctly and has a genuine need for additional supplies.

Arm title	NB-UVB

Arm description:

Placebo topical corticosteroid plus hand-held NB-UVB light

Arm type	Experimental

Investigational medicinal product name	placebo TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

same as active TCS

Arm title	Combination

Arm description:

topical corticosteroid plus hand held NB-UVB light

Arm type	Experimental
Investigational medicinal product name	TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

The total dosage needed by a participant over the course of the 9 month treatment phase is not expected to exceed 270g, and a procedure will be in place to capture any instances where a trial participant has requested more than this amount. Before being prescribed additional ointment, checks will be made to establish the need for additional supplies, and if necessary, a consultation with a dermatologist associated with the trial will be arranged to determine whether or not the participant is using the ointment correctly and has a genuine need for additional supplies.

Number of subjects in period 1	TCS ointment	NB-UVB	Combination
Started	173	169	175
Completed	173	169	175

Period 2

Period 2 title	follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	TCS ointment

Arm description:

topical corticosteroid plus dummy hand-held NB-UVB light

Arm type	Active comparator

Investigational medicinal product name	TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

The total dosage needed by a participant over the course of the 9 month treatment phase is not expected to exceed 270g, and a procedure will be in place to capture any instances where a trial participant has requested more than this amount. Before being prescribed additional ointment, checks will be made to establish the need for additional supplies, and if necessary, a consultation with a dermatologist associated with the trial will be arranged to determine whether or not the participant is using the ointment correctly and has a genuine need for additional supplies.

Arm title	NB-UVB

Arm description:

Placebo topical corticosteroid plus hand-held NB-UVB light

Arm type	Experimental
Investigational medicinal product name	placebo TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

same as active TCS

Arm title	Combination

Arm description:

topical corticosteroid plus hand held NB-UVB light

Arm type	Experimental
Investigational medicinal product name	TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

The total dosage needed by a participant over the course of the 9 month treatment phase is not expected to exceed 270g, and a procedure will be in place to capture any instances where a trial participant has requested more than this amount. Before being prescribed additional ointment, checks will be made to establish the need for additional supplies, and if necessary, a consultation with a dermatologist associated with the trial will be arranged to determine whether or not the participant is using the ointment correctly and has a genuine need for additional supplies.

Number of subjects in period 2	TCS ointment	NB-UVB	Combination
Started	173	169	175
Completed	119	123	128
Not completed	54	46	47
Consent withdrawn by subject	24	17	19
Adverse event, non-fatal	1	2	-
Lost to follow-up	27	24	24
not assessed	2	3	4

Baseline characteristics

Reporting groups	
Reporting group title	TCS ointment
Reporting group description:	
topical corticosteroid plus dummy hand-held NB-UVB light	
Reporting group title	NB-UVB
Reporting group description:	
Placebo topical corticosteroid plus hand-held NB-UVB light	
Reporting group title	Combination
Reporting group description:	
topical corticosteroid plus hand held NB-UVB light	

Reporting group values	TCS ointment	NB-UVB	Combination
Number of subjects	173	169	175
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)	22	22	27
Adolescents (12-17 years)	18	17	13
Adults (18-64 years)	120	115	120
From 65-84 years	13	15	15
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	38.6	36.9	37.0
standard deviation	± 20.0	± 18.9	± 19.1
Gender categorical			
Units: Subjects			
Female	98	81	70
Male	75	88	105

Reporting group values	Total		
Number of subjects	517		
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)	71		
Adolescents (12-17 years)	48		
Adults (18-64 years)	355		

From 65-84 years	43		
85 years and over	0		

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	249		
Male	268		

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants analysed as randomised, regardless of adherence with allocated group and without imputation of missing data.

Subject analysis set title	modified ITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

as randomised and without imputation of missing data

Reporting group values	ITT	modified ITT	
Number of subjects	517	370	
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)	71	61	
Adolescents (12-17 years)	48	38	
Adults (18-64 years)	355	234	
From 65-84 years	43	37	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	37.5	37.9	
standard deviation	± 19.3	± 20.5	
Gender categorical			
Units: Subjects			
Female	249	185	
Male	268	185	

End points

End points reporting groups

Reporting group title	TCS ointment
Reporting group description: topical corticosteroid plus dummy hand-held NB-UVB light	
Reporting group title	NB-UVB
Reporting group description: Placebo topical corticosteroid plus hand-held NB-UVB light	
Reporting group title	Combination
Reporting group description: topical corticosteroid plus hand held NB-UVB light	
Reporting group title	TCS ointment
Reporting group description: topical corticosteroid plus dummy hand-held NB-UVB light	
Reporting group title	NB-UVB
Reporting group description: Placebo topical corticosteroid plus hand-held NB-UVB light	
Reporting group title	Combination
Reporting group description: topical corticosteroid plus hand held NB-UVB light	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants analysed as randomised, regardless of adherence with allocated group and without imputation of missing data.	
Subject analysis set title	modified ITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: as randomised and without imputation of missing data	

Primary: VNS treatment success - ITT

End point title	VNS treatment success - ITT
End point description: treatment success derived from VNS scale assessed at 9 months	
End point type	Primary
End point timeframe: at 9 months	

End point values	TCS ointment	NB-UVB	Combination	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	173[1]	169	175	517
Units: one	20	27	34	81

Notes:

[1] - with imputation of missing data

Statistical analyses

Statistical analysis title	generalised estimating equations

Statistical analysis description:

This is showing the first part of the complete analysis, where the comparison is UVB vs TCS.

Comparison groups	TCS ointment v NB-UVB
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.29
Method	Mixed models analysis
Parameter estimate	Adjusted risk difference
Point estimate	0.052
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.044
upper limit	0.149

Notes:

[2] - a minimum clinically important difference of 15% is specified

Statistical analysis title	generalised estimating equations

Statistical analysis description:

This is to show the second part of the complete analysis for the primary outcome, where the comparison is combination VS TCS.

Comparison groups	TCS ointment v Combination
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.032
Method	Mixed models analysis
Parameter estimate	Adjusted risk difference
Point estimate	0.109
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.209

Notes:

[3] - a target difference of 15% risk difference

Primary: VNS treatment success - modified ITT

End point title	VNS treatment success - modified ITT

End point description:

End point type	Primary

End point timeframe:

baseline to 9 months

End point values	TCS ointment	NB-UVB	Combination	modified ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	119	123	128	370[4]
Units: one	20	27	34	81

Notes:

[4] - without imputation of missing data

Statistical analyses

Statistical analysis title	generalised estimating equations

Statistical analysis description:

without imputation of missing data at 9 months.
first part of complete analysis where comparison is UVB vs TCS.

Comparison groups	NB-UVB v TCS ointment
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.34
Method	Mixed models analysis
Parameter estimate	Adjusted risk difference
Point estimate	0.043
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.13

Notes:

[5] - without imputation of missing data

Statistical analysis title	generalised estimating equations

Statistical analysis description:

without imputation of missing data at 9 months.
first part of complete analysis where comparison is Combination vs TCS.

Comparison groups	TCS ointment v Combination
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Mixed models analysis
Parameter estimate	Adjusted risk difference
Point estimate	0.089
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.005
upper limit	0.184

Secondary: VNS treatment success - PPI

End point title	VNS treatment success - PPI

End point description:

End point type	Secondary

End point timeframe:

baseline to 9 months

End point values	TCS ointment	NB-UVB	Combination	modified ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	112[6]	108	116	336
Units: one	12	22	32	66

Notes:

[6] - without imputation of missing data

Statistical analyses

Statistical analysis title	generalised estimating equations

Statistical analysis description:

without imputation of missing data at 9 months.
first part of complete analysis where comparison is UVB vs TCS.

Comparison groups	TCS ointment v NB-UVB
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Mixed models analysis
Parameter estimate	Adjusted risk difference
Point estimate	0.097
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.012
upper limit	0.182

Statistical analysis title	generalised estimating equations

Statistical analysis description:

without imputation of missing data at 9 months.
first part of complete analysis where comparison is Combination vs TCS.

Comparison groups	TCS ointment v Combination

Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Adjusted risk difference
Point estimate	0.163
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.256

Secondary: Success from percentage repigmentation by blinded clinician

End point title	Success from percentage repigmentation by blinded clinician

End point description:

End point type	Secondary

End point timeframe:

9 months

End point values	TCS ointment	NB-UVB	Combination	modified ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	115	116	120	351[7]
Units: one	4	9	18	31

Notes:

[7] - without imputation of missing data

Statistical analyses

Statistical analysis title	mixed effects logistic regression

Statistical analysis description:

for comparison UVB vs TCS

Comparison groups	TCS ointment v NB-UVB
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.198
Method	Mixed models analysis
Parameter estimate	Adjusted odds ratio
Point estimate	2.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	7.51

Statistical analysis title	mixed effects logistic regression
Statistical analysis description: for comparison Combination vs TCS	
Comparison groups	TCS ointment v Combination
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Adjusted odds ratio
Point estimate	4.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	14.24

Secondary: Onset of treatment response

End point title	Onset of treatment response
End point description:	
End point type	Secondary
End point timeframe: by 9 months	

End point values	TCS ointment	NB-UVB	Combination	modified ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	141	138	149	428[8]
Units: one	138	136	145	419

Notes:
[8] - without imputation of missing data

Statistical analyses

Statistical analysis title	mixed effects logistic regression
Statistical analysis description: for comparison UVB vs TCS	
Comparison groups	TCS ointment v NB-UVB

Number of subjects included in analysis	279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Mixed models analysis
Parameter estimate	Adjusted odds ratio
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	11.62

Statistical analysis title	mixed effects logistic regression
Statistical analysis description: for comparison Combination vs TCS	
Comparison groups	TCS ointment v Combination
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.907
Method	Mixed models analysis
Parameter estimate	Adjusted odds ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	28.81

Secondary: Success from percentage repigmentation by nurse	
End point title	Success from percentage repigmentation by nurse
End point description: for target patch only	
End point type	Secondary
End point timeframe: at 9 months	

End point values	TCS ointment	NB-UVB	Combination	modified ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	115	115	119	349[9]
Units: one	10	11	21	42

Notes:

[9] - without imputation of missing data

Statistical analyses

Statistical analysis title	mixed effects logistic regression
Statistical analysis description: for comparison UVB vs TCS	
Comparison groups	TCS ointment v NB-UVB
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.774
Method	Mixed models analysis
Parameter estimate	Adjusted odds ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	2.32

Statistical analysis title	mixed effects logistic regression
Statistical analysis description: for comparison Combination vs TCS	
Comparison groups	TCS ointment v Combination
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	Adjusted odds ratio
Point estimate	2.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	4.15

Adverse events

Adverse events information	
Timeframe for reporting adverse events: between baseline and 9 months	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18
Reporting groups	
Reporting group title	TCS ointment
Reporting group description: -	
Reporting group title	NB-UVB
Reporting group description: -	
Reporting group title	Combination
Reporting group description: -	

Serious adverse events	TCS ointment	NB-UVB	Combination
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 173 (1.16%)	2 / 169 (1.18%)	1 / 175 (0.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
injury, poisoning and procedural complication			
subjects affected / exposed	1 / 173 (0.58%)	0 / 169 (0.00%)	0 / 175 (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
Nervous system disorders			
nervous system disorder			
subjects affected / exposed	0 / 173 (0.00%)	0 / 169 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gatrointestinal disorders			
subjects affected / exposed	0 / 173 (0.00%)	1 / 169 (0.59%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			

disorders			
respiratory, thoracic and mediastinal disorder			
subjects affected / exposed	0 / 173 (0.00%)	1 / 169 (0.59%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
infection and infestation			
subjects affected / exposed	1 / 173 (0.58%)	0 / 169 (0.00%)	0 / 175 (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: 0.05 %

Non-serious adverse events	TCS ointment	NB-UVB	Combination
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 173 (13.87%)	48 / 169 (28.40%)	52 / 175 (29.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
neoplasms benign, malignant and unspecified			
subjects affected / exposed	0 / 173 (0.00%)	2 / 169 (1.18%)	1 / 175 (0.57%)
occurrences (all)	0	2	1
Injury, poisoning and procedural complications			
injury, poisoning and procedural			
subjects affected / exposed	1 / 173 (0.58%)	0 / 169 (0.00%)	2 / 175 (1.14%)
occurrences (all)	1	0	2
Vascular disorders			
vascular disorder			
subjects affected / exposed	0 / 173 (0.00%)	1 / 169 (0.59%)	3 / 175 (1.71%)
occurrences (all)	0	1	3
Nervous system disorders			
nervous system disorder			
subjects affected / exposed	0 / 173 (0.00%)	0 / 169 (0.00%)	1 / 175 (0.57%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
general disorder			

subjects affected / exposed	0 / 173 (0.00%)	2 / 169 (1.18%)	0 / 175 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	0 / 173 (0.00%)	0 / 169 (0.00%)	2 / 175 (1.14%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
respiratory, thoracic and mediastinal disorder			
subjects affected / exposed	1 / 173 (0.58%)	0 / 169 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
skin and subcutaneous tissue disorder			
subjects affected / exposed	21 / 173 (12.14%)	45 / 169 (26.63%)	50 / 175 (28.57%)
occurrences (all)	29	58	85
Musculoskeletal and connective tissue disorders			
musculoskeletal and connective tissue			
subjects affected / exposed	1 / 173 (0.58%)	0 / 169 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Infections and infestations			
infection and infestation			
subjects affected / exposed	1 / 173 (0.58%)	4 / 169 (2.37%)	6 / 175 (3.43%)
occurrences (all)	1	6	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2015	Amended Typos and added details of the MRC START sub-study; Added REC details and clinical information red the MED test; Amended so sites can add info about where the medical photography department is; Updated to allow the nurse at site to write some free text / or draw a diagram to direct the participant to their medical photography department; Updated for clarity and to reflect changes to the diary data collection
25 September 2015	Addition of four new sites to Part C of the IRAS form
30 September 2015	Inclusion and Exclusion updates; more details for treatment training, digital image analysis, allocation blinding; Changes to AE handling for erythema;
15 March 2017	Amendment to protocol to accommodate nested process evaluation and increase in trial sample size. Addition of documentation to be used for nested process evaluation. Addition of documents to aid retention.
23 May 2017	Change of PI at Royal Wolverhampton Trust (site 01) from Dr Seau Tak Cheung to Dr Walter Machado
18 January 2018	Changes to the protocol - Sponsor address updated - Trial Pharmacist changed - Changes have been made to document that some participants will received the study feedback and quality of life questionnaires at an earlier time point, due to shorten trial timelines. Some participants will receive these questions as part of their 15 or 18 month questionnaire (whichever is received last) as opposed to the 21 month questionnaire. - Addition of potential further output testing of some used devices. - Change to primary outcome analysis due to lower than expected retention
26 April 2018	Change of PI at site 15 Middlesbrough from Dr Robert Ellis to Dr Azad (South Tees Trust)
16 July 2018	Change of PI at site 01, Cannock, from Dr Machado to Dr Hamad (Royal Wolverhampton Trust) AND Change of PI at site 10, Derby, from Dr Batchelor to Dr Ferguson

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.

na

Notes: