Clinical trial results:
Aprepitant – effect and safety in treatment of atopic dermatitis

Summary

EudraCT number	2013-002029-40
Trial protocol	SE
Global end of trial date	31 March 2015

Results information

Result version number	v1 (current)
This version publication date	10 April 2021
First version publication date	10 April 2021

Trial information

Trial identification

Sponsor protocol code	1001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	17177, Stockholm, Sweden,
Public contact	Dep of dermatology, Karolinska Univ, Karolinska institutet, klas.nordlind@karolinska.se
Scientific contact	Dep of dermatology, Karolinska Univ, Karolinska institutet, klas.nordlind@karolinska.se

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	31 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2015
Global end of trial reached?	Yes
Global end of trial date	31 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of Aprepitant (Emend) on atpoic dermatitis and prutitus.

Protection of trial subjects:

The protocol was approved by the local ethics committee and by the Medical Products Agency. Safety was assessed by recording adverse events at the second visit. The patients could also contact the clinic at any time during the treatment period if they observed any suspected side-effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2013
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	Sweden: 39
Worldwide total number of subjects	39
EEA total number of subjects	39

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)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited from dermatology clinics in the Stockholm area and examined at the Department of Dermatology, Karolinska University Hospital, Solna, Stockholm, Sweden, between October 2013 to March 2015.

Pre-assignment

Screening details:

Patients had a moderate–severe (SCORAD > 20) AD and diagnosis was determined according to the Williams criteria. Exclusion criteria: other concomitant diseases or medications (except for contraceptives), skin type 5–6 according to Fitzpatrick, skin infections, pregnancy, breast-feeding. The washout period for prior systemic treatment was 2 months.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group

Arm description:

The patients received 80 mg/day of aprepitant orally for 7 days in addition to standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.
21 participants were enrolled, but 2 of those patients interrupted study treatment due to adverse events, specifically experienced transient side-effects, such as dizziness, impotence, headache (1 case) and lack of reactivity, dyspnoea and palpitations (the second case). Those 2 patients are not included in the baseline characteristics or analysis that is presented here.

Arm type	Experimental
Investigational medicinal product name	Aprepitant
Investigational medicinal product code	SUB20017
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

80 mg/day of aprepitant orally for 7 days.

Investigational medicinal product name	Hydrocortisone butyrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden).

Arm title	Control group

Arm description:

Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.

Arm type	Standard topical treatment

Investigational medicinal product name	Hydrocortisone butyrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden).

Number of subjects in period 1	Treatment group	Control group
Started	19	20
Completed	19	20

Baseline characteristics

Reporting groups	
Reporting group title	Treatment group
Reporting group description:	
The patients received 80 mg/day of aprepitant orally for 7 days in addition to standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer. 21 participants were enrolled, but 2 of those patients interrupted study treatment due to adverse events, specifically experienced transient side-effects, such as dizziness, impotence, headache (1 case) and lack of reactivity, dyspnoea and palpitations (the second case). Those 2 patients are not included in the baseline characteristics or analysis that is presented here.	
Reporting group title	Control group
Reporting group description:	
Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.	

Reporting group values	Treatment group	Control group	Total
Number of subjects	19	20	39
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)	19	20	39
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	30.8	29.3	
standard deviation	± 8.4	± 9.2	-
Gender categorical Units: Subjects			
Female	7	16	23
Male	12	4	16
OSCORAD			
OSCORAD = objective SCORing of Atopic Dermatitis			
Units: Score			
arithmetic mean	40.5	37.0	
standard deviation	± 12.0	± 11.3	-
Visual analogue scale Units: Score			
arithmetic mean	5.5	6.7	
standard deviation	± 2.1	± 2.2	-
IgE levels Units: kU/l			

arithmetic mean	903.7	876.5	
standard deviation	± 1.391	± 1.934	-
Scratching movements			
Units: Registered number daily			
arithmetic mean	77.3	65.0	
standard deviation	± 97.9	± 100.9	-
Montgomery Åsberg Depression Rating Scale			
Units: Score			
arithmetic mean	5.6	9.3	
standard deviation	± 4.9	± 8.9	-
Hospital Anxiety and Depressive scale			
Units: Score			
arithmetic mean	3.4	6.6	
standard deviation	± 4.1	± 4.8	-
Substance P			
Units: pmol/g			
arithmetic mean	98.7	105.6	
standard deviation	± 54.4	± 46.5	-

End points

End points reporting groups

Reporting group title	Treatment group
Reporting group description:	
The patients received 80 mg/day of aprepitant orally for 7 days in addition to standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer. 21 participants were enrolled, but 2 of those patients interrupted study treatment due to adverse events, specifically experienced transient side-effects, such as dizziness, impotence, headache (1 case) and lack of reactivity, dyspnoea and palpitations (the second case). Those 2 patients are not included in the baseline characteristics or analysis that is presented here.	
Reporting group title	Control group
Reporting group description:	
Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.	

Primary: OSCORAD Post-treatment

End point title	OSCORAD Post-treatment
End point description:	
Objective SCORing of Atopic Dermatitis, arbitrary units (range 0–83)	
End point type	Primary
End point timeframe:	
Day 7 of treatment.	

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Score				
arithmetic mean (standard deviation)	32.0 (± 11.2)	26.7 (± 14.7)		

Statistical analyses

Statistical analysis title	Difference OSCORAD post-treatment
Statistical analysis description:	
Difference in OSCORAD between treatment and control after 7 days of treatment.	
Comparison groups	Treatment group v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	t-test, 2-sided

Secondary: Visual analogue scale Post-treatment

End point title	Visual analogue scale Post-treatment
End point description:	
Visual analogue scale, arbitrary units (range 0–10).	
End point type	Secondary
End point timeframe:	
Day 7 of treatment.	

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Score				
arithmetic mean (standard deviation)	3.8 (± 2.2)	4.1 (± 3.0)		

Statistical analyses

Statistical analysis title	Difference VAS post-treatment
Statistical analysis description:	
Difference in Visual Analogue Scale between treatment and control after 7 days of treatment.	

Comparison groups	Treatment group v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	t-test, 2-sided

Secondary: IgE levels Post-treatment

End point title	IgE levels Post-treatment
End point description:	

End point type	Secondary
End point timeframe:	
Day 7 of treatment.	

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: kE/l				
arithmetic mean (standard deviation)	937.9 (± 1.403)	821.1 (± 1.754)		

Statistical analyses

Statistical analysis title	Difference IgE levels post treatment
Statistical analysis description: Difference in IgE levels between treatment and control after 7 days of treatment.	
Comparison groups	Treatment group v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Scratching movements Post-treatment

End point title	Scratching movements Post-treatment
End point description:	
End point type	Secondary
End point timeframe: Day 7 of treatment.	

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Registered number daily				
arithmetic mean (standard deviation)	48.3 (± 62.6)	34.7 (± 45.0)		

Statistical analyses

Statistical analysis title	Difference Scratching movements post-treatment
Statistical analysis description: Difference in Scratching movements between treatment and control after 7 days of treatment.	
Comparison groups	Treatment group v Control group

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	t-test, 2-sided

Secondary: Montgomery Åsberg Depression Rating Scale Post-treatment

End point title	Montgomery Åsberg Depression Rating Scale Post-treatment

End point description:

Montgomery Åsberg Depression Rating Scale, arbitrary units (range 0–54).

End point type	Secondary

End point timeframe:

Day 7 of treatment.

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Score				
arithmetic mean (standard deviation)	4.0 (± 5.3)	6.5 (± 5.9)		

Statistical analyses

Statistical analysis title	Difference Depression scale post-treatment

Statistical analysis description:

Difference in Montgomery Åsberg Depression Rating Scale between treatment and control after 7 days of treatment.

Comparison groups	Treatment group v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	t-test, 2-sided

Secondary: HAD Post-treatment

End point title	HAD Post-treatment

End point description:

Hospital Anxiety and Depressive scale, arbitrary units (range 0–21).

End point type	Secondary

End point timeframe:

Day 7 of treatment.

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Score				
arithmetic mean (standard deviation)	3.5 (± 3.2)	4.8 (± 3.7)		

Statistical analyses

Statistical analysis title	Difference HAD post-treatment
Statistical analysis description: Difference in HAD between treatment and control after 7 days of treatment.	
Comparison groups	Treatment group v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	t-test, 2-sided

Secondary: Substance P Post-treatment

End point title	Substance P Post-treatment
End point description:	
End point type	Secondary
End point timeframe: Day 7 of treatment.	

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: pmol/g				
arithmetic mean (standard deviation)	97.6 (± 50.3)	91.0 (± 32.7)		

Statistical analyses

Statistical analysis title	Difference Substance P post-treatment

Statistical analysis description:

Difference in Substance P between treatment and control after 7 days of treatment.

Comparison groups	Treatment group v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study start to day 7 of treatment.

Adverse event reporting additional description:

Recording of adverse events was done at the second visit (day 7 of treatment). The patients could also contact the clinic at any time during the treatment period if they observed any suspected side-effects. No frequency threshold was used, as all adverse events that arise were reported.

Assessment type	Systematic

Dictionary used

Dictionary name	ICD
Dictionary version	10-SE

Reporting groups

Reporting group title	Treatment group
Reporting group description: -	
Reporting group title	Control group

Reporting group description: -

Serious adverse events	Treatment group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Treatment group	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 21 (61.90%)	0 / 20 (0.00%)	
Product issues			
Headache, fatigue, dizziness, elevated liver enzymes, palpitations, dyspnoea...	Additional description: 13/21 participants in treatment reported trancient AE: headache, fatigue, dizziness, elevated liver enzymes, palpitations, dyspnoea, altered ability to react, obstipation, stomach-ache, periocular dermatitis, erectile dysfunction, lack of reactivity.		
subjects affected / exposed	13 / 21 (61.90%)	0 / 20 (0.00%)	
occurrences (all)	13	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Patients in this study generally did not have worse than moderate pruritus, which may have had an impact on the results. There were different sex distributions in the 2 groups, thus it cannot be excluded that aprepitant exerts sex-specific effects.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29182791