Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Parallel Group Clinical Study to Assess the Safety and Efficacy of Three Doses of Clobetasol Propionate when Administered Intra-orally Twice Daily in Patients with Oral Lichen Planus (OLP) using Rivelin®-CLO patches

Summary

EudraCT number	2017-002193-40
Trial protocol	IE DK GB
Global end of trial date	20 December 2019

Results information

Result version number	v1 (current)
This version publication date	11 November 2021
First version publication date	11 November 2021
Summary attachment (see zip file)	Full CSR (DT-OLP_CSR_final_1.0_20200629.pdf) CSR Summary (DT-OLP_CSR_final_1.0_20200629_Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	DT-001-R-004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Afyx Therapeutics A/S
Sponsor organisation address	Lergravsvej 57, 2. tv, København S, Denmark,
Public contact	Lars Siim Madsen, PhD, Afyx Therapeutics A/S, +45 51912315, lsm@afyxtx.com
Scientific contact	Lars Siim Madsen, PhD, Afyx Therapeutics A/S, +45 51912315, lsm@afyxtx.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	12 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2019
Global end of trial reached?	Yes
Global end of trial date	20 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of three different doses of Rivelin®-CLO patches in treating OLP lesions over 4 weeks of treatment assessed by change in ulcer area.

Protection of trial subjects:

While patients were encouraged to complete the study, they had the right to discontinue from IMP or completely withdraw from the study at any time and for any reason without disclosing why and without having disadvantages. A genuine effort had to be made to determine the reason(s) why patient decided to discontinue IMP treatment or withdraw from the study, whenever possible.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
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: 27
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Ireland: 10
Country: Number of subjects enrolled	Canada: 29
Country: Number of subjects enrolled	United States: 52
Worldwide total number of subjects	138
EEA total number of subjects	30

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)	82
From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After having provided written informed consent, the patients underwent screening procedures. This could include a study biopsy in case OLP had not been histologically confirmed in the past. At the end of the screening period, eligible patients were randomly assigned to one of the treatment groups on Day 0 (Visit 2/Baseline).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Arm 1

Arm description:

Rivelin®-CLO 1 µg/patch

Arm type	Experimental
Investigational medicinal product name	Rivelin®-CLO
Investigational medicinal product code	
Other name	Clobetasol propionate
Pharmaceutical forms	Oromucosal patch
Routes of administration	Oral use, Topical

Dosage and administration details:

1 µg/patch

Arm title	Treatment Arm 2

Arm description:

Rivelin®-CLO 5 µg/patch

Arm type	Experimental
Investigational medicinal product name	Rivelin®-CLO
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal patch
Routes of administration	Oral use, Topical

Dosage and administration details:

5 µg/patch

Arm title	Treatment Arm 3

Arm description:

Rivelin®-CLO 20 µg/patch

Arm type	Experimental
Investigational medicinal product name	Rivelin®-CLO
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal patch
Routes of administration	Oral use, Topical

Dosage and administration details:
20 µg/patch

Arm title	Placebo
Arm description: Rivelin® plain patch (Placebo)	
Arm type	Placebo
Investigational medicinal product name	Rivelin®-CLO 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal patch
Routes of administration	Oral use, Topical

Dosage and administration details:
0 µg/patch (placebo)

Number of subjects in period 1	Treatment Arm 1	Treatment Arm 2	Treatment Arm 3
Started	40	34	33
Completed	34	33	30
Not completed	6	1	3
Consent withdrawn by subject	1	-	2
Adverse event, non-fatal	2	-	-
Other reason	1	-	-
Lost to follow-up	1	-	-
Lack of efficacy	1	1	-
Protocol deviation	-	-	1

Number of subjects in period 1	Placebo
Started	31
Completed	25
Not completed	6
Consent withdrawn by subject	2
Adverse event, non-fatal	2
Other reason	-
Lost to follow-up	-
Lack of efficacy	2
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Arm 1
Reporting group description: Rivelin®-CLO 1 µg/patch	
Reporting group title	Treatment Arm 2
Reporting group description: Rivelin®-CLO 5 µg/patch	
Reporting group title	Treatment Arm 3
Reporting group description: Rivelin®-CLO 20 µg/patch	
Reporting group title	Placebo
Reporting group description: Rivelin® plain patch (Placebo)	

Reporting group values	Treatment Arm 1	Treatment Arm 2	Treatment Arm 3
Number of subjects	40	34	33
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 Units: years			
median	63	61	60
full range (min-max)	19 to 89	37 to 75	33 to 77
Gender categorical Units: Subjects			
Female	28	21	24
Male	12	13	9
Race Units: Subjects			
White	36	32	26
Black or afro-am.	2	0	1
Asian	2	1	4
Native American	0	1	0
Other	0	0	2

Reporting group values	Placebo	Total	
Number of subjects	31	138	

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 Units: years			
median	66		
full range (min-max)	30 to 81	-	
Gender categorical Units: Subjects			
Female	26	99	
Male	5	39	
Race Units: Subjects			
White	29	123	
Black or afro-am.	1	4	
Asian	1	8	
Native American	0	1	
Other	0	2	

End points

End points reporting groups	
Reporting group title	Treatment Arm 1
Reporting group description: Rivelin®-CLO 1 µg/patch	
Reporting group title	Treatment Arm 2
Reporting group description: Rivelin®-CLO 5 µg/patch	
Reporting group title	Treatment Arm 3
Reporting group description: Rivelin®-CLO 20 µg/patch	
Reporting group title	Placebo
Reporting group description: Rivelin® plain patch (Placebo)	

Primary: Primary Efficacy Endpoint	
End point title	Primary Efficacy Endpoint
End point description:	
End point type	Primary
End point timeframe: Baseline to average of week 3 and 4.	

End point values	Treatment Arm 1	Treatment Arm 2	Treatment Arm 3	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	34	33	31
Units: Area (cm^2)				
number (confidence interval 95%)				
Week 3-4	-0.19 (-0.61 to 0.22)	-0.51 (-0.95 to -0.07)	-0.45 (-0.89 to -0.01)	0.06 (-0.38 to 0.50)

Statistical analyses

Statistical analysis title	Analysis of ulcer size (cm^2), ANCOVA, FAS
Comparison groups	Treatment Arm 1 v Treatment Arm 2 v Treatment Arm 3 v Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0468 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	-0.01
Variability estimate	Standard deviation
Dispersion value	0.87

Notes:

[1] - Significance level changed to 0.049 (adjusted for interim analysis)
5 mcg to placebo, p value = 0.0226
1 mcg vs placebo, p value = 0.3579

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For the safety analysis all AEs occurring from first trial-related activity performed until the end of the trial had been recorded and were coded and sorted by MedDRA-System Organ Class (SOC) and preferred terms (PT).

Adverse event reporting additional description:

In the safety analysis all AEs in the Safety Set (N=138) are displayed by treatment group. Multiple occurrences of AEs related to a particular SOC or PT, respectively, in the same patient count as one occurrence.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Treatment Arm 1
Reporting group description:	
Rivelin®-CLO 1 µg/patch	
Reporting group title	Treatment Arm 2
Reporting group description:	
Rivelin®-CLO 5 µg/patch	
Reporting group title	Treatment Arm 3
Reporting group description:	
Rivelin®-CLO 20 µg/patch	
Reporting group title	Placebo
Reporting group description:	
Rivelin® plain patch (Placebo)	

Serious adverse events	Treatment Arm 1	Treatment Arm 2	Treatment Arm 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	0 / 34 (0.00%)	1 / 33 (3.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events		0	0
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	1 / 40 (2.50%)	0 / 34 (0.00%)	0 / 33 (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
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 40 (0.00%)	0 / 34 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment Arm 1	Treatment Arm 2	Treatment Arm 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 40 (10.00%)	4 / 34 (11.76%)	4 / 33 (12.12%)
Gastrointestinal disorders			
Periodontal disease			
subjects affected / exposed	2 / 40 (5.00%)	2 / 34 (5.88%)	4 / 33 (12.12%)
occurrences (all)	2	2	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 40 (5.00%)	2 / 34 (5.88%)	0 / 33 (0.00%)
occurrences (all)	2	2	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 31 (16.13%)		

Gastrointestinal disorders Periodontal disease subjects affected / exposed occurrences (all)	 2 / 31 (6.45%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 3 / 31 (9.68%) 3		

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