Clinical trial results:
Pilot study of vulval lichen sclerosus treatment by adipose tissue associated with autologous platelet-rich plasma

Summary

EudraCT number	2016-003952-63
Trial protocol	ES
Global end of trial date	12 December 2020

Results information

Result version number	v1 (current)
This version publication date	12 February 2022
First version publication date	12 February 2022

Trial information

Trial identification

Sponsor protocol code	LIQUENIA

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Instituto de Investigación Sanitaria La Fe de Valencia
Sponsor organisation address	Avenida Fernando Abril Martorell, Torre 106 A 7planta, 46026 València, , Valencia, Spain,
Public contact	Jose Maria Millan Salvador, Instituto de Investigación Sanitaria La Fe, investigacion_clinica@iislafe.es
Scientific contact	Jose Maria Millan Salvador, Instituto de Investigación Sanitaria La Fe, investigacion_clinica@iislafe.es

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	02 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 December 2020
Global end of trial reached?	Yes
Global end of trial date	12 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate the improvement in the elasticity of the fibrosis plaques of patients affected by vulval lichen sclerosus after two infiltrations of fat tissue and autologous platelet-rich plasma.

Protection of trial subjects:

The reference study was conducted in Spain under the legal framework of Royal Decree 1090/2015. It has been performed in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, adopted by the General Assembly of the World Medical Association (1996). In addition, the study has been conducted in accordance with the protocol, good clinical practice (GCP) in accordance with the guidelines of the international conference on harmonization (ICH) and regulatory requirements for participating institutions.

An appropriately performed informed consent has been used, in compliance with GCP according to ICH guidelines and approved by the CEIm of the Hospital Universitario y Politécnico La Fe. Prior to inclusion of subjects in the study, a copy of the CEIm-approved informed consent has been reviewed with the prospective participant, signed and dated. The investigator has provided a copy of each subject's signed informed consent form and has retained a copy in the subject's study file.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 September 2017
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	Spain: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	19
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

• Start of patient inclusion: September 2017
• Completion of inclusion of patients: March 2018
• Patient follow-up time: 12 months.
• Expected completion date of the last patient included: March 2019.

Pre-assignment

Screening details:

• Adult women between 18 and 70 years of age.
• Patients with a clear clinical and/or histological diagnosis of lichen sclerosus (LE).
• Moderate or severe involvement of the disease at the genital level.
• Patients who have received topical treatment for at least three months with 0.05% clobetasol propionate.
• Prior signed informed consent

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Control

Arm description:

maintenance treatment of topical corticosteroid therapy (clobetasol 0.05%) to be administered as per usual clinical practice.

Arm type	Normal treatment
Investigational medicinal product name	clobetasol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Reference treatment, dose and mode of administration: Clobetasol propionate 0.05%.
Route of administration: topical
Dosage: 1 application per day, twice a week.

Arm title	Treatment group

Arm description:

2 infiltrations separated by three months will be applied by intra and subdermal injection in each vulvar half with identical amount of treatment composed of autologous fat tissue (10cc) enriched with autologous platelet-rich plasma (2cc).

Arm type	Experimental
Investigational medicinal product name	Autologous adipose tissue
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Intra and subdermal injection in each vulvar half of 20cc of autologous fatty tissue + 4cc of autologous platelet-rich plasma.

Number of subjects in period 1	Control	Treatment group
Started	10	10
Completed	10	9
Not completed	0	1
discontinued intervention	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Control
Reporting group description:	
maintenance treatment of topical corticosteroid therapy (clobetasol 0.05%) to be administered as per usual clinical practice.	
Reporting group title	Treatment group
Reporting group description:	
2 infiltrations separated by three months will be applied by intra and subdermal injection in each vulvar half with identical amount of treatment composed of autologous fat tissue (10cc) enriched with autologous platelet-rich plasma (2cc).	

Reporting group values	Control	Treatment group	Total
Number of subjects	10	10	20
Age categorical			
Adult women between 18 and 70 years of age.			
Units: Subjects			
Adults 18-70 years	10	10	20
Gender categorical Units: Subjects			
Female	10	10	20

End points

End points reporting groups

Reporting group title	Control
Reporting group description: maintenance treatment of topical corticosteroid therapy (clobetasol 0.05%) to be administered as per usual clinical practice.	
Reporting group title	Treatment group
Reporting group description: 2 infiltrations separated by three months will be applied by intra and subdermal injection in each vulvar half with identical amount of treatment composed of autologous fat tissue (10cc) enriched with autologous platelet-rich plasma (2cc).	

Primary: Elasticity of the fibrotic plaques in the affected vulvar area

End point title	Elasticity of the fibrotic plaques in the affected vulvar area
End point description:	
End point type	Primary
End point timeframe: 12 moths	

End point values	Control	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Number				
arithmetic mean (standard deviation)				
Baseline	0.57 (± 0.19)	0.63 (± 0.12)		
12 months	0.65 (± 0.18)	0.68 (± 0.12)		

Statistical analyses

Statistical analysis title	T-Test
Statistical analysis description: Categorical variables were described as absolute counts and percentages, while continuous variables were described as means and standard deviations. The efficacy analysis was based on the per-protocol principle—defined as all the randomized patients without major protocol violations that met the inclusion criteria who received the scheduled study medication and completed the efficacy measurements both at baseline and at 12 months. The baseline characteristics of both groups were compared,	
Comparison groups	Control v Treatment group

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	0.86
Confidence interval	
level	95 %
sides	1-sided
lower limit	0
Variability estimate	Standard deviation

Notes:

[1] - For continuous variables, Student’s t tests were used for normal data or Mann–Whitney U tests were employed otherwise. Data symmetry was analyzed using the Shapiro–Wilk normality test. Mann–Whitney U tests were used for group comparisons. Histological changes were evaluated by using Wilcoxon matched-pairs signed-rank tests. All the statistical tests used to evaluate the treatment effects were 1-sided and were considered statistically significant when the P values were\0.05. All the stat

Secondary: Pain

End point title	Pain
End point description:	
End point type	Secondary
End point timeframe:	
12 moths	

End point values	Control	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Number				
arithmetic mean (standard deviation)				
Baseline	2.3 (± 3)	5.3 (± 3.9)		
1 year	3.6 (± 3.5)	1.3 (± 1.4)		

Statistical analyses

Statistical analysis title	t-Student
Comparison groups	Control v Treatment group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	0.077

Confidence interval	
level	95 %
sides	1-sided
lower limit	0

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The investigator recorded in the CRD all the adverse events that occurred in the patients who participated in the clinical trial. AEs were followed up by the investigator and documented on the CRF up to 28 days after the end of the treatment period.

Adverse event reporting additional description:

The SAEs were notified by the investigator to the sponsor when he became aware of it

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

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

Reporting group description: -

Serious adverse events	Control	Treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Control	Treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 10 (100.00%)	
Investigations			
New diagnosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	1	
Vascular disorders			
Trombidiasis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	40	40	
Surgical and medical procedures			

Varicose vein subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 40	1 / 10 (10.00%) 40	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 40	4 / 10 (40.00%) 40	
Skin and subcutaneous tissue disorders Vulvar Liche Sclerosis subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 40	0 / 10 (0.00%) 40	
Endocrine disorders Biliary cirrhosis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 40	0 / 10 (0.00%) 40	
Musculoskeletal and connective tissue disorders Low back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Fracture subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 40 2 / 10 (20.00%) 40 2 / 10 (20.00%) 40	1 / 10 (10.00%) 40 1 / 10 (10.00%) 40 0 / 10 (0.00%) 40	
Infections and infestations Respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Gastrointestinal infection subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 7 4 / 10 (40.00%) 40 3 / 10 (30.00%) 40	2 / 10 (20.00%) 7 1 / 10 (10.00%) 40 1 / 10 (10.00%) 40	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35048150