Clinical trial results:
Comparative Study, intraindividual to evaluate efficacy and safety of the treatment of actinic keratosis with photodinamic therapy between methyl aminolevulinate cream and aminolevulinic acid nanosome gel

Summary

EudraCT number	2015-002408-97
Trial protocol	ES
Global end of trial date	21 June 2016

Results information

Result version number	v1 (current)
This version publication date	28 June 2021
First version publication date	28 June 2021

Trial information

Trial identification

Sponsor protocol code	MALvsALA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02647151
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Carlos Serra - Fundación Instituto Valenciano de Oncología
Sponsor organisation address	C/. Profesor Beltrán Baguena, n.º 8 , Valencia, Spain, 46009
Public contact	Federico Nepote, Marketing Farmacéutico & Investigación Clinica, 0034 934344412, investigacion@mfar.net
Scientific contact	Federico Nepote, Marketing Farmacéutico & Investigación Clinica, 0034 934344412, investigacion@mfar.net

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	21 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2016
Global end of trial reached?	Yes
Global end of trial date	21 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare MAL with the new photosensitizer BF-200 ALA in terms of local reaction and tolerability of the QA treatment

Protection of trial subjects:

All procedures were performed in accordance to Good clinical practice guidelines, the ICH principles for development of clinical research derived from the declaration of Helsinki and its later update fortaleza 2013. This clinical trial was approved by the local competent authorities in Spain and was developed in compliance to the current local regulations in terms of clinical research and data protection.
The protocol already includes measures to mitigate risk and protection of subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 August 2015
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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	12
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In order to achieve masking of the treatment by the researchers, the initial visit where the patient's data was collected and the treatment area was randomly assigned to each of the photosensitizers, was carried out by a different dermatologist from the one who evaluated the variables of the study

Period 1

Period 1 title	Whole study period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

In order to achieve masking of the treatment by the researchers, the initial visit where the patient's data was collected and the treatment area was randomly assigned to each of the photosensitizers, was carried out by a different dermatologist from the one who evaluated the variables of the study

Arms

Are arms mutually exclusive?	No
Arm title	BF-200 ALA

Arm description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.
The patients were administered with BF-200 ALA in the allocated region.

Arm type	Experimental
Investigational medicinal product name	BF-200 ALA
Investigational medicinal product code	ATC: L01XD04
Other name	Ameluz 78 mg/g gel
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

1 aplication previos to phototherapy. 78 mg/g

Arm title	MAL cream

Arm description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.
The patients were administered with MAL in the allocated region.

Arm type	Active comparator
Investigational medicinal product name	MAL
Investigational medicinal product code	ATC: L01X D03
Other name	Metvix 160 mg/g cream
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

1 dose administration. 160 mg/g

Number of subjects in period 1	BF-200 ALA	MAL cream
Started	22	22
Completed	22	22

Baseline characteristics

Reporting groups	
Reporting group title	Whole study period

Reporting group description: -

Reporting group values	Whole study period	Total	
Number of subjects	22	22	
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			
Patient age at inclusion			
Units: years			
log mean	72		
full range (min-max)	57 to 84	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	21	21	
Treatment region			
Body region where the patient was treated. Each patient received both treatments in simetric and similar body regions			
Units: Subjects			
scalp	12	12	
forehead	6	6	
cheek	4	4	

End points

End points reporting groups

Reporting group title	BF-200 ALA
Reporting group description:	
Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions. The patients were administered with BF-200 ALA in the allocated region.	
Reporting group title	MAL cream
Reporting group description:	
Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions. The patients were administered with MAL in the allocated region.	

Primary: Immediate local reaction

End point title	Immediate local reaction
End point description:	
The immediate local reaction to illumination may include, to a greater or lesser degree, erythema, inflammation, and edema. It will be scored on a scale from 0 to 10 where 0 will be normal skin, without local reaction and 10 a maximum local reaction.	
End point type	Primary
End point timeframe:	
First visit, treatment administration	

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Arbitary unit				
arithmetic mean (standard deviation)	5.4 (± 1.96)	4.7 (± 1.96)		

Statistical analyses

Statistical analysis title	ANOVA 1 factor
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.255
Method	ANOVA

Primary: Late local reaction

End point title	Late local reaction

End point description:

The late local reaction defined by the presence to a greater or lesser degree of erythema, inflammation, edema, scabs and pustules, will also be scored from 0 to 10 where 0 will be normal skin, no local reaction and 10 a maximum local reaction.

End point type	Primary

End point timeframe:

Second visit (day 2-3 after treatment administration)

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Arbitary unit				
arithmetic mean (standard deviation)	7.4 (± 1.92)	5.9 (± 1.92)		

Statistical analyses

Statistical analysis title	ANOVA 1 factor
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.049
Method	ANOVA

Primary: Pain

End point title	Pain

End point description:

Pain experienced by patients is measured using a subjective, 10-cm visual analog scale. The most frequent symptoms are pain and burning sensations on the skin, beginning during lighting or shortly after, and lasting a few hours, usually resolving on the day of treatment. The severity is normally mild to moderate, and rarely, requires a premature interruption of lighting.

End point type	Primary

End point timeframe:

First visit, treatment administration

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Arbitary unit				
arithmetic mean (standard deviation)	5.2 (± 2.6)	5 (± 2.6)		

Statistical analyses

Statistical analysis title	ANOVA 1 factor
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.956
Method	ANOVA

Secondary: Qeratosis lesion number on each patient

End point title	Qeratosis lesion number on each patient
End point description: extension of the treated lesions	
End point type	Secondary
End point timeframe: Baseline	

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: number of lesions				
arithmetic mean (standard deviation)	13.4 (± 4.4)	14.7 (± 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fluorescence emission

End point title	Fluorescence emission
End point description: Fluorescence will be studied with a Wood light lamp immediately before illumination and this can be scored from 0 to 10, where 0 was an absolute absence of fluorescence, 5 a limited and selective fluorescence in the QA lesions and 10 a fluorescence in the entire treatment area where the photosensitizer had been applied .	
End point type	Secondary
End point timeframe: Selection visit	

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Arbitary unit				
arithmetic mean (standard deviation)	6.9 (± 2.01)	5.3 (± 2.01)		

Statistical analyses

Statistical analysis title	1 factor ANOVA
Statistical analysis description:	
Descriptive comparison between two means and SD.	
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.026
Method	ANOVA

Secondary: Treatment satisfaction

End point title	Treatment satisfaction
End point description:	
The patients will be asked about the satisfaction provided by the treatment in each of the areas (benefit obtained in relation to the discomfort and discomfort of the treatment) to obtain an answer in the form of a score from 0 to 10 where 0 is absolutely dissatisfied and 10 Totally satisfied.	
End point type	Secondary
End point timeframe:	
Visit 3, 30 days after treatment administration	

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Arbitary unit				
arithmetic mean (standard deviation)	7.5 (± 3.8)	7.4 (± 3.8)		

Statistical analyses

Statistical analysis title	ANOVA 1 factor
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.938
Method	ANOVA

Secondary: Percentage of resolved Qeratosis lesions (QAs)

End point title	Percentage of resolved Qeratosis lesions (QAs)
End point description:	
Percentage of queratosis lesions resolved.	
End point type	Secondary
End point timeframe:	
visit 3, 30 days after treatment administration	

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Number of lesions				
Resolved	84	81		
Not resolved	16	19		

Statistical analyses

Statistical analysis title	ANOVA 1 factor
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7012
Method	ANOVA

Secondary: Clinical response to treatment

End point title	Clinical response to treatment
End point description:	
The clinical response will be assessed with the help of the initial photograph and the transparent template. Partial response (PR) is defined if ≥75% of the initial AKs are resolved and complete response (CR) if 100% of them are resolved.	
End point type	Secondary

End point timeframe:
Visit 3, 30 days after treatment administration

End point values	BF-200 ALA	MAL cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: patients				
Complete response	13	11		
Partial response	5	7		
No response	4	4		

Statistical analyses

Statistical analysis title	Complete response comparison between arms
Statistical analysis description:	
The percentage of patients with complete response was compared between treatment arms	
Comparison groups	MAL cream v BF-200 ALA
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5448
Method	ANOVA

Statistical analysis title	Partial response comparison between arms
Statistical analysis description:	
The percentage of patients with partial response among treatment arms was compared	
Comparison groups	BF-200 ALA v MAL cream
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.735
Method	ANOVA

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The sponsor collected adverse events (AEs) up to 30 days after administration of the last dose of study treatment.

Adverse event reporting additional description:

Patients experienced no adverse events during the 30 days of participation in this trail.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	BF-200 ALA

Reporting group description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.
The patients were administered with BF-200 ALA in the allocated region.

Reporting group title	MAL cream

Reporting group description:

Treatment was randomly and blindly assigned to a lesion. All patients received both treatment but in different regions.
The patients were administered with MAL in the allocated region.

Serious adverse events	BF-200 ALA	MAL cream	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	BF-200 ALA	MAL cream	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: We confirm there were no Adverse events reported throughout the trial. This is consistent with the type of treatment, the pathology and the study design

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