Clinical trial results:
RANDOMISED PILOT STUDY TO ASSESS THE CLINICAL EFFICACY OF DAYLIGHT PHOTODYNAMIC THERAPY WITH METHYL AMINOLEVULINATE CREAM (METVIX?), (MAL-PDT), IN THE PREVENTION OF ACTINIC KERATOSIS AND NON MELANOMA SKIN CANCER IN TRANSPLANT PATIENTS

Summary

EudraCT number	2015-002663-42
Trial protocol	ES
Global end of trial date	25 October 2018

Results information

Result version number	v1 (current)
This version publication date	20 October 2021
First version publication date	20 October 2021
Summary attachment (see zip file)	Final report summary (INFORME FINAL 17-06-2019. FIRMADO.pdf)

Trial information

Trial identification

Sponsor protocol code	TFDTRASP

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Clínica Universidad de Navarra
Sponsor organisation address	Avda. Pío XII, 36, Pamplona, Spain, 31008
Public contact	UCEC, Clínica Universidad de Navarra, 34 9482554002725, ucicec@unav.es
Scientific contact	UCEC, Clínica Universidad de Navarra, 34 9482554002725, ucicec@unav.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 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2018
Global end of trial reached?	Yes
Global end of trial date	25 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess if there are less appearance of AK in the side treated with repeated treatments of daylight photodynamic therapy compared with the side treated with cryotherapy, in transplant patients, at 21 months from treatment initiation.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	4
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 24 patients were included. Three patients were lost. One after the first intervention and two after the 3-month visit. All treatment and follow-up visits were completed by 21 patients. All patients were male and Caucasian.

Pre-assignment

Screening details:

Recruitment started in April 2016 and ended in February 2017.
25 patients were selected, of which 24 were included. One patient was not finally included because he did not meet the inclusion criteria.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Blind for evaluator and not blind for the patient and the doctor.

Arms

Arm title	Treatment

Arm description:

This study has an intra-individual comparison design, in which a half-face was treated with MAL-PDT in daylight and the contralateral side was the control in each patient. The control side was treated with cryotherapy, which is the best treatment option for now, and is what is commonly used to treat actinic keratoses in these types of patients. This design, therefore, is not a crossover design since each treatment was applied to a different area at the same time. It is a design commonly used in dermatology for the comparison of topical treatments.

The sides of the face and / or the scalp were randomly assigned to the interventions based on a computer generated sequence. Each patient was assigned an order number.

Arm type	Experimental
Investigational medicinal product name	metil-aminolevulinato (MAL) in combination with Photodynamic therapy (PDT)
Investigational medicinal product code	
Other name	Metvix
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

1st Treatment at most 3 weeks after inclusion: TFD-MAL with daylight of a half face and Cryotherapy (2 freezing cycles) on the contralateral side on the day of initiation of treatment.
2nd Treatment carried out 3 months after the first treatment: TFD-MAL with daylight of a half face and Cryotherapy (2 freezing cycles) on the contralateral side on the day of initiation of treatment.
3rd Treatment: carried out 9 months after the first treatment: TFD-MAL with daylight of a half face and Cryotherapy (2 freezing cycles) on the contralateral side on the day of initiation of treatment.

Number of subjects in period 1	Treatment
Started	24
Completed	21
Not completed	3
Consent withdrawn by subject	3

Baseline characteristics

Reporting groups	
Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
Adults (18-64 years)	4	4	
From 65-84 years	20	20	
Gender categorical Units: Subjects			
Female	0	0	
Male	24	24	

End points

End points reporting groups

Reporting group title	Treatment

Reporting group description:

This study has an intra-individual comparison design, in which a half-face was treated with MAL-PDT in daylight and the contralateral side was the control in each patient. The control side was treated with cryotherapy, which is the best treatment option for now, and is what is commonly used to treat actinic keratoses in these types of patients. This design, therefore, is not a crossover design since each treatment was applied to a different area at the same time. It is a design commonly used in dermatology for the comparison of topical treatments.

The sides of the face and / or the scalp were randomly assigned to the interventions based on a computer generated sequence. Each patient was assigned an order number.

Primary: Difference in the number of total lesions between the two treatment areas at the final visit

End point title	Difference in the number of total lesions between the two treatment areas at the final visit[1]

End point description:

Difference in the number of total lesions between the two treatment areas at the final visit, V21, observed in the physical examination performed at that visit, compared to the pretreatment physical examination.

End point type	Primary

End point timeframe:

21 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this primary end point because there is only one group treatment and the end point is meassure of the difetrence number of lessions before and after the clinical trial.
All the variables were analyzed using the Student's t test for paired data or the Wilcoxon test of signed ranges for paired data. The cut-off point for establishing statistical significance was 0.05. All analyzes were performed using Stata 14 (StataCorp. 2015).

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: number	21			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

21 months

Assessment type	Systematic

Dictionary used

Dictionary name	NA
Dictionary version	NA

Reporting groups

Reporting group title	Treatment

Reporting group description: -

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 24 (41.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
cellulitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Fever			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Dyspnea and edema in the legs			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
unstable angina			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Decompensated heart failure			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Diffuse B lymphoma in jejunum			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Cognitive deterioration	Additional description: Subacute cognitive deterioration detected in visit on August 8, 2016		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
acute diverticulitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudoaneurysm bleeding			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)		

Cardiac disorders coronary stent placement subjects affected / exposed occurrences (all)	 1 / 24 (4.17%) 1		
General disorders and administration site conditions Headache subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) heatstroke subjects affected / exposed occurrences (all)	 2 / 24 (8.33%) 2 3 / 24 (12.50%) 3 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1		
Social circumstances Accidental fall subjects affected / exposed occurrences (all)	 1 / 24 (4.17%) 1		
Eye disorders Cataract surgery subjects affected / exposed occurrences (all) vitreous hemorrhage subjects affected / exposed occurrences (all) Loss of sight subjects affected / exposed occurrences (all)	 2 / 24 (8.33%) 2 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1		
Gastrointestinal disorders Diarrhoea			

subjects affected / exposed occurrences (all) Diverticulitis subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2 1 / 24 (4.17%) 1		
Respiratory, thoracic and mediastinal disorders bronchitis subjects affected / exposed occurrences (all)	 2 / 24 (8.33%) 2		
Skin and subcutaneous tissue disorders itchiness subjects affected / exposed occurrences (all) blisters subjects affected / exposed occurrences (all) Scabs subjects affected / exposed occurrences (all) desquamation subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Stinging subjects affected / exposed occurrences (all) Squamous cell carcinoma removal subjects affected / exposed occurrences (all) impetiginization subjects affected / exposed occurrences (all)	 5 / 24 (20.83%) 6 1 / 24 (4.17%) 1 7 / 24 (29.17%) 7 6 / 24 (25.00%) 6 12 / 24 (50.00%) 12 7 / 24 (29.17%) 7 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1		
Musculoskeletal and connective tissue disorders			

Hip arthrosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Edema			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Gout			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Hernia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
laminectomy			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Thrombosed fistula removal			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Infections and infestations			
Common cold			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Flu			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	7		
Herpes dermatitis			

subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
Sialadenitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2016	modificate some aspects about the recruitmen, inclusion criteria and withdrawal
16 January 2018	Include a partial statistical analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported