Clinical trial results:
Comparison of Efficacy and Safety of Metvixia® Natural Daylight Photodynamic Therapy Versus Conventional Metvixia® Photodynamic Therapy in patients With grade I and II actinic keratosis of the scalp: a phase III trial

Summary

EudraCT number	2014-003602-32
Trial protocol	FR
Global end of trial date	22 December 2016

Results information

Result version number	v1 (current)
This version publication date	01 May 2021
First version publication date	01 May 2021
Summary attachment (see zip file)	2014-003602-32_results summary (DAYLIGHT-résume rapport final.pdf) 2014-003602-32_publication (2014-003602-32_publication.pdf)

Trial information

Trial identification

Sponsor protocol code	I14034/Daylight-PDT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02373371
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Limoges
Sponsor organisation address	2 Avenue Martin Lutrher King, Limoges, France, 87042
Public contact	Project manager, CHU de Limoges, 33 5 55 05 86 16 , abdeslam.bentaleb@chu-limoges.fr
Scientific contact	Dr Safae ASSIKAR, Investigator, CHU de Limoges, 33 05 55 05 5555, safae.assikar@chu-limoges.fr

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	14 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2016
Global end of trial reached?	Yes
Global end of trial date	22 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate clinical efficacy of daylight photodynamic therapy using Metvixia®compared to conventional PDT treatment using Metvixia®

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable French regulations regarding ethical committee review, competent authority, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2014
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	France: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

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)	3
From 65 to 84 years	19
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

This monocentric study took place in France between March 2015 and December 2016.
Patients included in the study were aged over 18 years and suffered from mild actinic keratosis (AK) (defined as slightly palpable AK, better felt than seen) and possibly moderate AK (moderately thick, easily felt and seen). The patients also acted as controls.

Pre-assignment

Screening details:

Patients with at least two comparable fields of AK on the face and scalp, with a minimum of five AKs in each area, were eligible. Main exclusion criteria were pigmented lesions, hypertrophic AK, non-melanoma skin cancer, AK treatment in the last month.
The patients also acted as controls for the purpose of treatment comparison.

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	daylight

Arm description:

Scales and crusts were gently removed, and the entire treatment area was superficially scraped.
Metvixia* was applied in a 1-mm thick layer to the entire treatment area and was kept uncovered on the side exposed to daylight .
Patients exposed themselves continuously to daylight for 2 h, starting within 30 min of applying the MAL cream . Exposure to daylight was allowed if the weather was not rainy and if the temperature was above 10°C.

Arm type	Crossover
Investigational medicinal product name	Metvixia*
Investigational medicinal product code	
Other name	methyl aminolevulinate (MAL)
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Metvixia* 16% cream was applied in a 1-mm thick layer to the entire treatment area

Arm title	Blue light

Arm description:

Scales and crusts were gently removed, and the entire treatment area was superficially scraped.
Metvixia* was applied in a 1-mm thick layer to the entire treatment area and was covered. Patients started blue light exposure 3 h after the MAL cream was applied, using a Waldmann PDT (Herbert Waldmann GmbH & Co, Villingen-Schwenningen,
Germany) 450 lamp at 10 J/cm2. The median duration of illumination ranged from 15 to 18 min.

Arm type	Crossover
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Other name	methyl aminolevulinate (MAL)
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Routes of administration	Cutaneous use

Dosage and administration details:
Metvixia* 16% cream was applied in a 1-mm thick layer to the entire treatment area

Number of subjects in period 1	daylight	Blue light
Started	13	13
Completed	13	13

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	26	26	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	19	19	
85 years and over	3	3	
Gender categorical Units: Subjects			
Female	2	2	
Male	24	24	

End points

End points reporting groups

Reporting group title	daylight

Reporting group description:

Scales and crusts were gently removed, and the entire treatment area was superficially scraped. Metvixia* was applied in a 1-mm thick layer to the entire treatment area and was kept uncovered on the side exposed to daylight .
Patients exposed themselves continuously to daylight for 2 h, starting within 30 min of applying the MAL cream . Exposure to daylight was allowed if the weather was not rainy and if the temperature was above 10°C.

Reporting group title	Blue light

Reporting group description:

Scales and crusts were gently removed, and the entire treatment area was superficially scraped. Metvixia* was applied in a 1-mm thick layer to the entire treatment area and was covered. Patients started blue light exposure 3 h after the MAL cream was applied, using a Waldmann PDT (Herbert Waldmann GmbH & Co, Villingen-Schwenningen,
Germany) 450 lamp at 10 J/cm2. The median duration of illumination ranged from 15 to 18 min.

Primary: Percenatge of number of AK lesions cleared at the 3-month

End point title	Percenatge of number of AK lesions cleared at the 3-month

End point description:

End point type	Primary

End point timeframe:

At 3 months

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Number				
arithmetic mean (standard deviation)	19.6 (± 6)	20 (± 6.9)		

Statistical analyses

Statistical analysis title	Principal analysis

Statistical analysis description:

The main analysis is to compare at 3 month to e 0 the difference between the number of KA disappeared after Daylight PDTT and number of KA disappeared after Bluelight PDT) the 0 with a nonparametric test on paired data of signed Wilcoxon ranks.

Comparison groups	daylight v Blue light

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.846 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - The raw difference in the number of AK is not statistically different from 0 and the numbers of disappeared AK are not statistically significant between the two treatments

Primary: Recurrence of lesions at Week 4

End point title	Recurrence of lesions at Week 4[2]

End point description:

End point type	Primary

End point timeframe:

At Week 4

Notes:

[2] - 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 test was carried out because the 15% margin was no longer valid

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	1		
Units: number				
arithmetic mean (standard deviation)	0.3 (± 0.7)	0.2 (± 0.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Raw number of AK lesions cleared at week 4

End point title	Raw number of AK lesions cleared at week 4

End point description:

End point type	Secondary

End point timeframe:

At week 4

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Number				
arithmetic mean (standard deviation)	19.4 (± 6.1)	20.1 (± 6.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Raw number of AK lesions cleared at Week 24

End point title	Raw number of AK lesions cleared at Week 24

End point description:

End point type	Secondary

End point timeframe:

At Week 24

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Number				
arithmetic mean (standard deviation)	19.7 (± 6.2)	20.2 (± 7.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence of lesions at Week 12

End point title	Recurrence of lesions at Week 12

End point description:

End point type	Secondary

End point timeframe:

At Week 12

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	6		
Units: Number				
arithmetic mean (standard deviation)	1.2 (± 1.2)	0.5 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence of lesions at Week 24

End point title	Recurrence of lesions at Week 24

End point description:

End point type	Secondary

End point timeframe:

At Week 24

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	10		
Units: Number				
arithmetic mean (standard deviation)	2.4 (± 1.6)	1 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain assessment

End point title	Pain assessment

End point description:

The pain felt after each procedure, was evaluated using a numerical scale from 0 (no pain) to 10 (extreme pain).

End point type	Secondary

End point timeframe:

Pain recorder just after exposure to the light.

End point values	daylight	Blue light		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Number				
arithmetic mean (standard deviation)	1.2 (± 1.9)	5.1 (± 3.9)		

Statistical analyses

Statistical analysis title	Pain statistical analysis

Statistical analysis description:

The analysis consists in comparing with 0 the difference in pain felt after treatment with Daylight-PDT and BleuLight PDT.

Comparison groups	Blue light v daylight
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [3]
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - The pain felt after Daylight-PDT is significantly less than the pain felt after Blue light-PDT

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Adverse events were recorder from 15/10/2014 to 15/10/2017	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Bluelight
Reporting group description: -	

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: No non-serious adverse events were recorded . Pain was analyzed in the secondary end points.

Serious adverse events	Bluelight		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 26 (3.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Ischaemic stroke	Additional description: left facial paralysis with episode of transient dysarthria. Hospitalization for suspicion of transient ischemic attack, aphasia, language disorder, left paralysisdyarthria. Treatment with anti-platelet aggregation agent + kardegic 300 mg +tahor 20 mg		
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Bluelight		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)		

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/31955461