Clinical trial results:
Treatment of Actinic Keratoses with Ingenol Mebutate and topical glucocorticosteroid - a safety study

Summary

EudraCT number	2013-002583-80
Trial protocol	DK
Global end of trial date	28 January 2014

Results information

Result version number	v1 (current)
This version publication date	27 November 2021
First version publication date	27 November 2021
Summary attachment (see zip file)	Publication (Erlendsson_2016_JAAD.pdf)

Trial information

Trial identification

Sponsor protocol code	38814

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Dermatology, Bispebjerg University Hospital
Sponsor organisation address	Bispebjerg Bakke 23, Copenhagen, Denmark, 2400
Public contact	Clinical Trail Information, Department of Dermatology, Bispebjerg University Hospital, +45 60668830, andres.erlendsson@gmail.com
Scientific contact	Clinical Trail Information, Department of Dermatology, Bispebjerg University Hospital, +45 60668830, andres.erlendsson@gmail.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	28 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective is to investigate whether local skin responses seen after Picato® can be treated with a topical glucocorticosteroid. Secondary objective is to investigate if the treatment efficacy is affected by it. It is the perspective of this study to be offer patients safe treatment of local skin responses after Picato® treatment while maintaining an effective eradication of the Actinic Keratoses.

Protection of trial subjects:

Outlined in protocol. Field treatment often causes local skin responses and in the case of severe LSR a glucocorticosteroid would be administered in a normal clinical setting. The subject came to regular follow-ups to address any side effects and had a phone number to the treating physician they could call at any time in between visits.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 September 2013
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	Denmark: 21
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	7
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients, 18 years or older with multiple actinic keratosis and field cancerization in face or scalp were recruited for participation. Patients were recruited between September 2013 and November 2014 at Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark.

Pre-assignment

Screening details:

Patients refereed with actinic keratosis to Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark, were screened for participation. . Inclusion required two similar treatment areas of 25 cm2 containing a minimum of seven AKs on field-cancerized skin.

Pre-assignment period milestones

Number of subjects started	21
Number of subjects completed	21

Period 1

Period 1 title	STUDY PERIOD (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Investigator was blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	INT/CONTR

Arm description:

Each subject was its own control. Control: Ingenol mebutate. Intervention: Ingenol mebutate + clobetasol propionate

Arm type	INT/CONTR
Investigational medicinal product name	Picato
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	External use

Dosage and administration details:

Applied on day 1,2 and 3, or day 1 and 2.

Arm title	NULL

Arm description:

Made up arm because of faulty reporting system.

Arm type	NULL

No investigational medicinal product assigned in this arm

Number of subjects in period 1	INT/CONTR	NULL
Started	20	1
Completed	20	1

Baseline characteristics

Reporting groups	
Reporting group title	STUDY PERIOD

Reporting group description: -

Reporting group values	STUDY PERIOD	Total	
Number of subjects	21	21	
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)	7	7	
From 65-84 years	14	14	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	20	20	

End points

End points reporting groups	
Reporting group title	INT/CONTR
Reporting group description:	
Each subject was its own control. Control: Ingenol mebutate. Intervention: Ingenol mebutate + clobetasol propionate	
Reporting group title	NULL
Reporting group description:	
Made up arm because of faulty reporting system.	

Primary: Local skin response in control vs intervention day 4	
End point title	Local skin response in control vs intervention day 4
End point description:	
End point type	Primary
End point timeframe:	
Assessed days 1, 4, 8, 15, 57	

End point values	INT/CONTR	NULL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	1		
Units: LSR 0-24				
number (not applicable)	9.95	9.95		

Statistical analyses

Statistical analysis title	STAT
Comparison groups	INT/CONTR v NULL
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	9.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	9.37
upper limit	10.53
Variability estimate	Standard deviation

Notes:

[1] - Kolmogorov-Smirnov test indicated normal distribution for LSR, pain, and pruritus and was compared using paired t test. Wilcoxon signed rank test compared clearance rates and cosmetic outcome, while McNemar test compared paired ratios of complete clearance. Clearance of grade I to III AK was pooled for all patients and presented as clearance rates in the population. P values were 2-sided and considered statistically significant when less than .05.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

3 months

Adverse event reporting additional description:

Local skin responses were seen assessed at each visit. No clinical hypopigmentation or hyperpigmentation was observed. One patient got an E-coli/Enterococcal infection in the treatment area receiving ingenol mebutate + clobetasole, which after relevant antibiotic treatment left a cicatrix.

Assessment type	Non-systematic

Dictionary used

Dictionary name	CT-3
Dictionary version	2011

Reporting groups

Reporting group title	STUDY/CONTROL

Reporting group description:

Each subject was its own control. Control: Ingenol mebutate. Intervention: Ingenol mebutate + clobetasol propionate

Serious adverse events	STUDY/CONTROL		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	STUDY/CONTROL		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)		
Infections and infestations			
Adverse reaction	Additional description: E-coli infection in the skin of treated area. Assessed as a moderate adverse reaction (causes the patient discomfort) and needed therapeutic intervention. At follow up, a cicatrix was noted in the previously infected area.		
alternative assessment type: Systematic			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		

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