Clinical trial results:
Does 4% 5-fluorouracil pre-treatment improve the efficacy of daylight photodynamic therapy for actinic keratoses – a randomized controlled study

Summary

EudraCT number	2021-001586-21
Trial protocol	DK
Global end of trial date	06 December 2023

Results information

Result version number	v1 (current)
This version publication date	29 August 2024
First version publication date	29 August 2024

Trial information

Trial identification

Sponsor protocol code	5FUdPDT78842

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Dermatology, Bispebjerg Hospital
Sponsor organisation address	Nielsine Nielsens Vej 9, Copenhagen NV, Denmark, 2400
Public contact	Principal investigator, Bispebjerg Hospital, Department of Dermatology, stine.regin.wiegell@regionh.dk
Scientific contact	Principal investigator, Bispebjerg Hospital, Department of Dermatology, 0045 30914617, stine.regin.wiegell@regionh.dk

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	13 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 December 2023
Global end of trial reached?	Yes
Global end of trial date	06 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to compare the efficacy of sequential 4% 5-FU and daylight MAL-PDT with daylight MAL-PDT alone in the treatment of multiple actinic keratoses in the face and scalp

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Signed informed consent was obtained from all participants prior to entry into the study and the Good Clinical Practice Unit, Copenhagen University, performed external monitoring. The protocol was approved by the Danish Medicine Agency (EudraCT 2021-0015860-21), The Regional Ethics Committee of Region Hovedstaden (H-78842), and the Danish Data Protection Agency.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2021
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	9
From 65 to 84 years	48
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from October 2021 to November 2022

Pre-assignment

Screening details:

Patients referred to the Department of Dermatology, Bispebjerg University Hospital, Copenhagen (n=50) or Private Hospital Mølholm, Vejle, Denmark (n=10) for treatment of multiple AKs.

Pre-assignment period milestones

Number of subjects started	60
Number of subjects completed	60

Period 1

Period 1 title	Treatment and follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	5-FU dPDT

Arm description:

Patients applied 5-FU cream (Tolak® 40 mg/g, Pierre-Fabre Dermatologie, Boulogne, France) twice daily for 7 days. At day 7 MAL patients were treated with MAL-daylight PDT

Arm type	Experimental
Investigational medicinal product name	Tolak
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

twice daily for 7 days

Investigational medicinal product name	Metvix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

One treatment with daylight photodynamic therapy

Arm title	dPDT

Arm description:

At day 7 patients were treated with MAL-dPDT

Arm type	Active comparator

Investigational medicinal product name	Metvix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

One treatment with daylight photodynamic therapy

Number of subjects in period 1	5-FU dPDT	dPDT
Started	60	60
Completed	60	60

Baseline characteristics

Reporting groups	
Reporting group title	Treatment and follow-up
Reporting group description:	
Inter-individual design, split-face/scalp study	

Reporting group values	Treatment and follow-up	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
18-64 years	9	9	
65-84 years	48	48	
85 years and over	3	3	
Age continuous Units: years			
arithmetic mean	73		
full range (min-max)	56 to 89	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	54	54	

End points

End points reporting groups	
Reporting group title	5-FU dPDT
Reporting group description:	
Patients applied 5-FU cream (Tolak® 40 mg/g, Pierre-Fabre Dermatologie, Boulogne, France) twice daily for 7 days. At day 7 MAL patients were treated with MAL-daylight PDT	
Reporting group title	dPDT
Reporting group description:	
At day 7 patients were treated with MAL-dPDT	

Primary: Lesion response rate	
End point title	Lesion response rate
End point description:	
End point type	Primary
End point timeframe:	
3-month after treatment	

End point values	5-FU dPDT	dPDT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: %	87	75		

Statistical analyses

Statistical analysis title	Comparison
Comparison groups	5-FU dPDT v dPDT
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12-months	
Adverse event reporting additional description:	
Follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	5-FU dPDT
Reporting group description:	
Patients applied 5-FU cream (Tolak® 40 mg/g, Pierre-Fabre Dermatologie, Boulogne, France) twice daily for 7 days. At day 7 MAL patients were treated with MAL-daylight PDT	
Reporting group title	dPDT
Reporting group description:	
At day 7 patients were treated with MAL-dPDT	

Serious adverse events	5-FU dPDT	dPDT	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 60 (16.67%)	10 / 60 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
cancer coli			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Hypotension			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial flutter			
subjects affected / exposed	2 / 60 (3.33%)	2 / 60 (3.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
aorta valve repair			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 60 (3.33%)	2 / 60 (3.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aneurysm thrombosis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia and melaena			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudoaneurysm infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Stomach scan normal			
subjects affected / exposed	2 / 60 (3.33%)	2 / 60 (3.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			

subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polypectomy			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
fractured collumna			
subjects affected / exposed	1 / 60 (1.67%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	5-FU dPDT	dPDT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 60 (100.00%)	60 / 60 (100.00%)	
Skin and subcutaneous tissue disorders			
Erythema			
alternative assessment type: Non-systematic			
subjects affected / exposed	60 / 60 (100.00%)	60 / 60 (100.00%)	
occurrences (all)	60	60	

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