Clinical trial results:
Laser immunotherapy with and without topical anti-PD1 in basal cell carcinomas

Summary

EudraCT number	2019-003310-14
Trial protocol	DK
Global end of trial date	11 October 2021

Results information

Result version number	v1 (current)
This version publication date	16 June 2023
First version publication date	16 June 2023

Trial information

Trial identification

Sponsor protocol code	SHO20190708

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Dermatology
Sponsor organisation address	Bispebjerg bakke 23, Copenhagen, Denmark, 2400
Public contact	Department of Dermatology, Bispebjerg Hospital, 0045 38635000, silje.haukali.omland.01@regionh.dk
Scientific contact	Department of Dermatology, Bispebjerg Hospital, 0045 38635000, silje.haukali.omland.01@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	01 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2021
Global end of trial reached?	Yes
Global end of trial date	11 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study aim is to assess the immunological and clinical response in BCC treated with AFL or intratumoral nivolumab as monotherapy and compare with BCC treated with combination-therapy of AFL and the anti-PD1-drug Nivolumab (intratumoral).
Primary objectives
1. To investigate the immunological response of AFL or intratumoral nivolumab as monotherapy and AFL+Nivolumab (intratumoral) in BCC
2. To investigate the clinical response of AFL or nivolumab (intratumoral) as monotherapy and AFL+Nivolumab in BCC

Protection of trial subjects:

In case of Suspected Unexpected Serious Adverse Reactions (SUSARs), the study sponsor will immediately inform The Danish Medicines Agency and the Regional Committee on Health Research Ethics according to detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2020
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: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	6
From 65 to 84 years	20
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

In an undisturbed setting, the participant will be made aware of their right to have an assessor present, that participation is voluntary, and that withdrawal is possible at any time during the study. Participants will be given adequate consideration time (min 24 h). Participants will be asked to sign a consent form

Pre-assignment

Screening details:

- Patients 18 years or older
- Clinical suspicion of BCC or histologically verified BCC at baseline and histologically verified BCC at visit 2, irrespective of histologic subtype with diameter ≥7 mm at baseline.
- Signed informed consent.
- Female subjects of childbearing potential must be confirmed not pregnant by a negative pregnancy test

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Anti-PD1+AFL

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Opdivo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Injection

Dosage and administration details:

0.10 ml Nivolumab solution/cm2, intratumoral injection

Arm title	Arm_AFL

Arm description: -

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

Dosage and administration details:

0.1 ml per cm^2

Arm title	Anti-PD1

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Opdivo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Injection

Dosage and administration details:

0.10 ml Nivolumab solution/cm2, intratumoral injection

Number of subjects in period 1	Anti-PD1+AFL	Arm_AFL	Anti-PD1
Started	10	9	9
Completed	10	9	9

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
All patients included in the three groups	

Reporting group values	Overall trial	Total	
Number of subjects	28	28	
Age categorical			
18-100 years			
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)	6	6	
From 65-84 years	20	20	
85 years and over	2	2	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	18	18	

End points

End points reporting groups	
Reporting group title	Anti-PD1+AFL
Reporting group description: -	
Reporting group title	Arm_AFL
Reporting group description: -	
Reporting group title	Anti-PD1
Reporting group description: -	

Primary: Change in CD3+ T-cells	
End point title	Change in CD3+ T-cells
End point description: Primary objectives 1. To investigate the immunological response of AFL as monotherapy and AFL+Nivolumab in BCC 2. To investigate the clinical response of AFL as monotherapy and AFL+Nivolumab in BCC	
End point type	Primary
End point timeframe: End of trial	

End point values	Anti-PD1+AFL	Arm_AFL	Anti-PD1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: CD3+ cells				
arithmetic mean (standard deviation)	10 (± 2)	9 (± 2)	9 (± 2)	

Statistical analyses

Statistical analysis title	Comparison of CD3 positive cells
Comparison groups	Anti-PD1+AFL v Anti-PD1 v Arm_AFL
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Primary: Tumor reduction	
End point title	Tumor reduction
End point description: Primary objectives To investigate the clinical response of AFL as monotherapy and AFL+Nivolumab in BCC	
End point type	Primary
End point timeframe: End of trial	

End point values	Anti-PD1+AFL	Arm_AFL	Anti-PD1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: Tumor reduction				
number (not applicable)	10	9	9	

Statistical analyses

Statistical analysis title	Comparison of CD3+ cells before/after intervention
Statistical analysis description: The CD3+ cells were analyzed before and after intervention for all three intervention groups	
Comparison groups	Anti-PD1+AFL v Arm_AFL v Anti-PD1
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From intervention to end-of trial	
Adverse event reporting additional description:	
Local skin reaction	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	Local skin reactions
Dictionary version	1

Reporting groups	
Reporting group title	Anti-PD1+AFL
Reporting group description:	
Local skin reactions: all patients experienced local skin reactions consisting of either eythema, crusting og scaling one-week post-intervention. The skin reactions were reduced at month three, however some experienced hyperpigmentation to a mild degree	
Reporting group title	Arm_AFL
Reporting group description:	
Local skin reactions: all patients experienced mild local skin reactions consisting of either erythema, edema ,crusting og scaling one-week post-intervention. One patient had an infection at the intervention side that required oral anitbiotics. The skin reactions were reduced at month three. At month three one patient experienced hyperpigmentation to a mild degree.	
Reporting group title	Anti-PD1
Reporting group description:	
Local skin reactions: all patients experienced local skin reactions consisting of either erythema, crusting og scaling one-week post-intervention. The skin reactions were reduced or totally resolved at month three, however some experienced hyperpigmentation to a mild degree	

Serious adverse events	Anti-PD1+AFL	Arm_AFL	Anti-PD1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0		0

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Anti-PD1+AFL	Arm_AFL	Anti-PD1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
Infections and infestations			
Local skin infection	Additional description: One week after AFL treatment one patient developed a local skin oínfection at the intervention site that was treated with oral antibiotics.		

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0

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