Clinical trial results:
PHASE II INVESTIGATION OF CALCIUM ELECTROPORATION AS A TREATMENT FOR CUTANEOUS AND SUBCUTANEOUS MALIGNANT TUMOURS

Summary

EudraCT number	2019-004314-34
Trial protocol	DK DE
Global end of trial date	04 April 2023

Results information

Result version number	v1 (current)
This version publication date	03 November 2024
First version publication date	03 November 2024

Trial information

Trial identification

Sponsor protocol code	CaEP-R

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04225767
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zealand University Hospital
Sponsor organisation address	Ringstedgade 61, Næstved, Denmark,
Public contact	Lars Munch Larsen, Region Zealand, laml@regionsjaelland.dk
Scientific contact	Julie Gehl, Region Zealand, kgeh@regionsjaelland.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	04 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 October 2022
Global end of trial reached?	Yes
Global end of trial date	04 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of this study is to evaluate the clinical overall response rate of calcium electroporation treatment of malignant tumours of the skin after two months. The evaluation will use the modified RECIST criteria, clinical examination with calliper measurement and photographical documentation using adhesive rulers for scale. Response rate will be defined as number of responding lesions (partial or complete response) relative to treated lesions.

Protection of trial subjects:

Patients included had consented in writing and fulfilled all eligibility criteria. Standard safety monitoring was performed during treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 February 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 17
Country: Number of subjects enrolled	Germany: 2
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	12
From 65 to 84 years	6
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from three sites: Næstved (Denmark), Vejle (Denmark) and Lubeck (Germany).

Pre-assignment

Screening details:

Patients with any solid cancer and cutaneous metastases could be screened for inclusion. Patients could recieve other treatment, and could be included if there was no sign of regression of the cutaneous metastases - or progression.

Period 1

Period 1 title	inclusion, treatment and follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Experimental

Arm description:

Patients treated with intervention (Calcium electroporation)

Arm type	Experimental
Investigational medicinal product name	Calcium chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use

Dosage and administration details:

Tumors were measured (a longest diameter, b diameter perpendicular to a). A 3 mm margin was added. Calcium chloride was mixed to 220 mM (mixed with sodium chloride).

a. Tumour with a diameter <0.5 cm: 1 ml of calcium chloride solution pr cm3 tumour tissue was injected.
b. Tumour with a diameter from 0.5 cm to 3 cm: 0.5 ml of calcium chloride solution pr cm3 tumour tissue was injected.
(Maximum volume is 20 ml 220 mmol/l calcium chloride.)

Number of subjects in period 1	Experimental
Started	19
Completed	19

Baseline characteristics

Reporting groups	
Reporting group title	inclusion, treatment and follow-up

Reporting group description: -

Reporting group values	inclusion, treatment and follow-up	Total	
Number of subjects	19	19	
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)	12	12	
From 65-84 years	6	6	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	13	13	
Male	6	6	

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description:	
Patients treated with intervention (Calcium electroporation)	

Primary: Response at two months post treatment

End point title	Response at two months post treatment[1]
End point description:	
This EudraCT platform do not allow description at tumor level thus this has to be described in writing here. At the patient level (intention to treat) 6 of 19 patients experienced response at two months. Measuring according to tumors treated (58 tumors) the overall response rate was 36 % at the two months point.	
End point type	Primary
End point timeframe:	
Two months post treatment	

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: In this study percent of responding lesions (descriptive statistics) were used in the primary endpoint. 58 lesions were treated in 19 patients. Please see final publication.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: patients	19			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Study time period	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	Experimental

Reporting group description:

Patients treated with intervention (Calcium electroporation).
As non-serious adverse events is not an endpoint the numbers are those who experiencen AE's at two months
which are mentioned in the article: "Calcium electroporation in cutaneus metastases - A non-randomised phase II multicentre clinical trial"

Serious adverse events	Experimental		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis	Additional description: Patient had concomitant immunotherapy for lung cancer. Treatment area was inspected and there was no sign of infection. SAE deemed not related to therapy.		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis	Additional description: 11 months after treatment the patient get an infection in the tip of the Port-á-Cath (intravenous catheter). This was deemed not related to treatment.		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 19 (15.79%)		
Skin and subcutaneous tissue disorders			
Suppuration	Additional description: Discharge from cutaneuos metastases		
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Ulceration	Additional description: Ulcerated cutaneuos metastases/ulceration in treated areas		
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Pain cutaneous metastases	Additional description: Pain related to cutaneous metastases/treatment area		
subjects affected / exposed	1 / 19 (5.26%)		
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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37268521