Clinical trial results:
Calcium electroporation for the treatment of cutaneous metastases.

Summary

EudraCT number	2012-005704-17
Trial protocol	DK
Global end of trial date	23 January 2017

Results information

Result version number	v1 (current)
This version publication date	15 August 2021
First version publication date	15 August 2021

Trial information

Trial identification

Sponsor protocol code	AA1232

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01941901
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department of Oncology, University Hospital Herlev
Sponsor organisation address	Herlev Ringvej 75, Herlev, Denmark, 2730
Public contact	Department of Oncology, Herlev Hosp. In 2017 Julie Gehl changed position to Zealand Uni. Hosp., Department of Oncology, Herlev Hospital, 45 93577626, kgeh@regionsjaelland.dk
Scientific contact	Department of Oncology, Herlev Hosp. In 2017 Julie Gehl changed position to Zealand Uni. Hosp., Department of Oncology, Herlev Hospital, 45 93577626, 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	23 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2016
Global end of trial reached?	Yes
Global end of trial date	23 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate tumorresponse of calcium elctroporation and eletrochemotherapy with intratumoral bleomycin on cutaneous metastases, and compare the effect of the two treatments.

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	01 March 2013
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	Denmark: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	2
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from one site (Herlev Hospital).

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	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Assessor, Subject

Blinding implementation details:

Patients with cutaneous metastases were included in the study. The cutaneous metastases were identified by a number and measured. The measurements of these numbered metastases were given to the pharmacy unit through a hatch. The pharmacy mixed the correct volume of either calcium og bleomycin in one syringe per identified metastasis. Treatment proceded without the subject or investigator knowing whether the injected matter was calcium or bleomycin. At 6 monhts follow up the code was revealed.

Arms

Arm title	Treatment

Arm description:

All patients were treated. Individual metastases were assigned to either calcium electroporation or electroporation with bleomycin.

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:

The dose of calcium chloride was estimated from preclinical studies and set to 9 mg/ml (220 mmol/l). Initially, the injected volume for both bleomycin and calcium chloride were 0.5 ml/cm3 tumor volume. After treatment of five patients, the volume for the smaller tumors (0.5 cm3) was amended to 1 ml/cm3. Tumor volume was calculated as axbxbxpi/6, a = largest diameter, b = largest diameter perpendicular to a.

Investigational medicinal product name	bleomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intratumoral use

Dosage and administration details:

The dose of bleomycin was set to 1000 IU/ml in accordance with European Standard Operating Procedures for Electrochemotherapy (ESOPE). Initially, the injected volume for both bleomycin and calcium chloride were 0.5 ml/cm3 tumor volume. After treatment of five patients, the volume for the smaller tumors (0.5 cm3) was amended to 1 ml/cm3. Tumor volume was calculated as axbxbxpi/6, a = largest diameter, b = largest diameter perpendicular to a.

Number of subjects in period 1	Treatment
Started	7
Completed	7

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	7	7	
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)	2	2	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	7	7	
Male	0	0	

End points

End points reporting groups

Reporting group title	Treatment

Reporting group description:

All patients were treated. Individual metastases were assigned to either calcium electroporation or electroporation with bleomycin.

Primary: Response to treatment

End point title	Response to treatment[1]

End point description:

This reporting system does not allow reporting results from all treated metastases (as there a 7 subjects treated, but 37 metastases evaluated), which is the primary endpoint as reported in the paper listed. This endpoint reporting then lists the number of patients who have experienced response of treated lessions in the reporting period. Response is then that one or more treated metastases have at least a partial response (reduction of lesion by 30% or more, up to compete remission), and the number listed is the amount of patients which had at least one partial or complete response in the treated lesions.

End point type	Primary

End point timeframe:

6 months

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: The endpoint of this trial is based on evaluating treatment of 37 cutaneous metases, in 7 patients that each had one or more metastases. The paper from the study describes this including statistical analysis. It was not possible to report number of metastases across patients in the EudraCT reporting system, so we had to list the patients experiencing response.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: patients				
Patients with objective response of metastases	6			
Patients without objective response of metastases	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline through completion of last follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	Treatment

Reporting group description:

All patients were treated. Individual metastases were assigned to either calcium electroporation or electroporation with bleomycin.

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (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	Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Skin and subcutaneous tissue disorders			
ulceration	Additional description: ulceration of treated cutaneous metastasis (more than one metastasis could be treated in the same patient)		
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	4		
Itch	Additional description: Itching localized to the treated cutaneous metastases		
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
exudation	Additional description: Exudation of the cutaneous metastasis treated (more than one metastasis can be treated in each patient).		
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Hyperpigmentation			

subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3		

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/28816072