Clinical trial results:
Phase II trial: uPAR-PET for preoperative staging of breast cancer patients

Summary

EudraCT number	2015-004503-23
Trial protocol	DK
Global end of trial date	10 February 2017

Results information

Result version number	v1 (current)
This version publication date	01 January 2021
First version publication date	01 January 2021
Summary attachment (see zip file)	Status April 4 2018 (April 4 2018.docx) Status December 2020 - Results (Status December 2020.pdf)

Trial information

Trial identification

Sponsor protocol code	CS-2015-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02681640
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Professor Andreas Kjær, Rigshospitalet, Department of Clinical Physiology, Nuclear Medicine and PET, akjaer@sund.ku.dk
Scientific contact	Professor Andreas Kjær, Rigshospitalet, Department of Clinical Physiology, Nuclear Medicine and PET, akjaer@sund.ku.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 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 February 2017
Global end of trial reached?	Yes
Global end of trial date	10 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The sensitivity and specificity of 68Ga-NOTA-AE105 PET/CT for detection of lymph node metastases will be tested by observer-blinded readings (two separate teams) and compared to diagnostic performance of conventional preoperative diagnostic workup procedures. The reference test will be histopathology of lymph nodes obtained by operative lymph node dissection (SN/ALND). Primary end point dichotomized: +/- lymph node metastases in ipsilateral axilla

Protection of trial subjects:

This study was conducted in accordance with International Code of Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2016
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: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	31
From 65 to 84 years	19

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

50 patients were recruited at Rigshospitalet, Copenhagen University Hospital in the period Feburary 1 2016 to February 10 2017

Pre-assignment

Screening details:

54 patients were screened and were found eligible for inclusion in the study. However, 4 patients did not receive the radioligand due to technical failure of radioligand production and were excluded from the study

Period 1

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

Blinding implementation details:

observer-blinded readings of 68Ga-NOTA-AE105 PET/CT (two separate teams consisting of 1 experienced, board-certified specialist in Nuclear Medicine and 1 experienced, board-certified specialist in radiology

Arms

Arm title	Experimental arm

Arm description:

All included patients

Arm type	Experimental
Investigational medicinal product name	68Ga-NOTA-AE105
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

One injection of up to 200 Mbq

Number of subjects in period 1	Experimental arm
Started	50
Completed	49
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Intervention (overall period)

Reporting group description: -

Reporting group values	Intervention (overall period)	Total	
Number of subjects	50	50	
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)	18	18	
From 65-84 years	32	32	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	57		
standard deviation	± 13	-	
Gender categorical Units: Subjects			
Female	49	49	
Male	1	1	

End points

End points reporting groups

Reporting group title	Experimental arm
Reporting group description:	
All included patients	

Primary: Sensitivity and specificity of uPAR-PET (reader team 1)

End point title	Sensitivity and specificity of uPAR-PET (reader team 1)[1]
End point description:	
Sensitivity and specificity for detection of lymph node metastases on a per patient basis. Sensitivity (reader team 1): 37.0% [19.4-57.6%] Specificity (reader team 1): 86.4% [65.1-97.1%]	
End point type	Primary
End point timeframe:	
Whole study period	

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: Descriptive statistics included (95% CI) on sensitivity and specificity.
No statistical differences in sensitivity (team 1: uPAR-PET/CT vs. US+FNB: p=0.56; team 2: uPAR-PET/CT vs. US+FNB p=0.18) or specificity (team 1: uPAR-PET/CT vs. US+FNB p=0.08; Team 2: uPAR-PET/CT vs. US+FNB p=0.16) were found.

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: Patients				
True negative	19			
True positive	10			
False positive	3			
False negative	17			

Statistical analyses

No statistical analyses for this end point

Primary: Sensitivity and specificity of uPAR-PET (reader team 2)

End point title	Sensitivity and specificity of uPAR-PET (reader team 2)[2]
End point description:	
Sensitivity and specificity for detection of lymph node metastases on a per patient basis. Sensitivity (reader team 2): 29.6% [13.8-50.2%] Specificity (reader team 2): 90.9% [70.8-98.9%]	
End point type	Primary
End point timeframe:	
Whole study period	

Notes:

[2] - 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: Descriptive statistics included (95% CI) on sensitivity and specificity.
No statistical differences in sensitivity (team 1: uPAR-PET/CT vs. US+FNB: p=0.56; team 2: uPAR-PET/CT vs. US+FNB p=0.18) or specificity (team 1: uPAR-PET/CT vs. US+FNB p=0.08; Team 2: uPAR-PET/CT vs. US+FNB p=0.16) were found.

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: Patients				
True negative	20			
True positive	8			
False positive	2			
False negative	19			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

??? 2016 -10 Feb 2017

Adverse event reporting additional description:

Events was considered as related to the IMP if they occurred during the period from the time of injection of the tracer and up to 24 hours after the injection. Events / Adverse reactions occurring later than 24 hours after injection was not registered.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	All participants

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events were reported. This was as expected, as 68Ga-NOTA-AE105 has no known adverse effects

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
Anaphylactic reaction	Additional description: One patient developed anaphylactoid reactions to iodinated CT contrast media. The reaction started within 30 seconds after administration of the iodinated contrast media.		
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)		

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