



Clinical trial results:

Phase II trial: uPAR PET/CT and FDG PET/MRI for preoperative staging of bladder cancer

Summary

EudraCT number	2016-001026-33
Trial protocol	DK
Global end of trial date	04 December 2017

Results information

Result version number	v1 (current)
This version publication date	03 January 2021
First version publication date	03 January 2021

Trial information

Trial identification

Sponsor protocol code	AK2016-1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02805608
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Professor Andreas Kjaer, Rigshospitalet, Department of Clinical Physiology, Nuclear Medicine and PET, akjaer@sund.ku.dk
Scientific contact	Professor Andreas Kjaer, 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	18 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2017
Global end of trial reached?	Yes
Global end of trial date	04 December 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The sensitivity and specificity of 68Ga-NOTA-AE105 PET/CT and FDG PET/MR for detection of regional lymph node metastases will be tested by observer-blinded readings (two separate teams) and compared to diagnostic performance of conventional preoperative procedure. The reference test will be histopathology of lymph nodes obtained by operative lymph node dissection based on 6 regions. The suspected lymph nodes will be assigned to 6 regions based on the images. During the following operation the lymph nodes will be removed and analysed in each of these regions.

Protection of trial subjects:

An experienced medical doctor will be present in the department during the entire duration of the PET/CT and PET/MR scans. Emergency equipment is available in accordance with the current procedures of the department, including cardiopulmonary resuscitation and oxygen supply/suction. It is emphasized, that handling of emergency situations is part of the department's routine procedures, and the staff is trained

to handle e.g. unexpected allergic reactions associated with administration of CT contrast agents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2016
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from 10 DEC 2016 to 04 DEC 2017. All patients were recruited from Rigshospitalet, Denmark.

Pre-assignment

Screening details:

Screening performed by a medical doctor according to the inclusion and exclusion criteria

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?	No
Arm title	Experimental: uPAR PET/CT

Arm description:

Subjects injected with [68Ga]-NOTA-AE105 and subsequently scanned with PET/CT (uPAR PET/CT)

Arm type	Experimental
Investigational medicinal product name	[68Ga]-NOTA-AE105
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Dose of approximately 200 MBq (40 µg) administered intra-venously approximately 20 minutes prior to the PET/CT

Arm title	Experimental: FDG PET/MR
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Arm description:

Subjects injected with [18F]-FDG and subsequently scanned with PET/MR (FDG PET/MR)

Arm type	Experimental
Investigational medicinal product name	[18F]-FDG
Investigational medicinal product code	
Other name	2-Deoxy-2-[18F]fluoroglucose
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Dose of approximately 200 MBq administered intra-venously approximately 1 hour prior PET/MR

Number of subjects in period 1	Experimental: uPAR PET/CT	Experimental: FDG PET/MR
Started	14	11
Completed	14	10
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	18	18	
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)	6	6	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	66.3		
standard deviation	± 8.8	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	13	13	

End points

End points reporting groups

Reporting group title	Experimental: uPAR PET/CT
Reporting group description:	
Subjects injected with [68Ga]-NOTA-AE105 and subsequently scanned with PET/CT (uPAR PET/CT)	
Reporting group title	Experimental: FDG PET/MR
Reporting group description:	
Subjects injected with [18F]-FDG and subsequently scanned with PET/MR (FDG PET/MR)	

Primary: Sensitivity in detection of regional lymph node metastases

End point title	Sensitivity in detection of regional lymph node metastases ^{[1][2]}
End point description:	
Sensitivity of uPAR-PET/CT detection of regional lymph node metastases by 68Ga-NOTA-AE105 PET/CT	
End point type	Primary
End point timeframe:	
Evaluated on the uPAR PET/CT 20 minutes after injection of [68Ga]-NOTA-AE105	

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: uPAR-PET Image technical check following 18 patients, demonstrated that bladder cancer/lymph node metastases could not be discriminated from spillover caused by high bladder activity. Accordingly, the study was terminated prematurely.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The sensitivity for detection of regional lymph node metastases was also not performed for FDG PET/MR because the main purpose of the trial was to study the sensitivity of uPAR PET/CT. For technical reasons, this was not possible and the study was terminated prematurely. The number of included subjects at termination was too low for any meaningful analysis of FDG PET/MR sensitivity.

End point values	Experimental: uPAR PET/CT			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[3]			
Units: patients				
True positive				
False positive				
True negative				
False negative				

Notes:

[3] - Analysis not possible due to bladder spillover

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event are recorded from injection of IMP up to 24 hours after injection.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	5
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Reporting groups

Reporting group title	Experimental: uPAR PET/CT
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Reporting group description:

Subjects injected with [68Ga]-NOTA-AE105 and subsequently scanned with PET/CT (uPAR PET/CT)

Reporting group title	FDG PET/MR
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Reporting group description:

Subjects injected with [18F]-FDG and subsequently scanned with PET/MR (FDG PET/MR)

Serious adverse events	Experimental: uPAR PET/CT	FDG PET/MR	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Experimental: uPAR PET/CT	FDG PET/MR	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
General disorders and administration site conditions			
Claustrophobia	Additional description: Subject experienced claustrophobia and could not continue with the FDG PET/MR scan. Adverse event was not considered related to the IMP ([18F]-FDG)		
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2016	Change in production method of [68Ga]-NOTA-AE105

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

uPAR-PET Image technical check following 18 patients, demonstrated that bladder cancer/lymph node metastases could not be discriminated from spillover caused by high bladder activity. Accordingly, the study was terminated prematurely.

Notes: