Clinical trial results:
PET/CT imaging of uPAR-expression in patients with neuroendocrine tumors using 68Ga-NOTA-AE105

Summary

EudraCT number	2017-002312-13
Trial protocol	DK
Global end of trial date	08 July 2021

Results information

Result version number	v1 (current)
This version publication date	17 July 2022
First version publication date	17 July 2022

Trial information

Trial identification

Sponsor protocol code	AK2017-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03278275
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, 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, 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	08 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2021
Global end of trial reached?	Yes
Global end of trial date	08 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In this study with uPAR PET we include patients diagnosed with neuroendocrine tumors in order to investigate the tumor visualization and prognostic performance of (68Ga-NOTA-AE105) uPAR PET/CT

Protection of trial subjects:

It is emphasized that participation in the study is voluntary and will have no influence on the otherwise planned treatment, whether the patient will participate or not. The study is conducted in accordance with the Helsinki Declaration and the Good Clinical Practice (GCP). All clinical information about the participants is protected under the act on processing of Personal Data and the Danish Health Legislation. Overall, it is considered that the project is ethically sound, as there are no significant risks associated with the uPAR PET/CT imaging procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2017
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: 116
Worldwide total number of subjects	116
EEA total number of subjects	116

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)	47
From 65 to 84 years	69

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Prospective inclusion patients with lung or gastro-entero-pancreatic neuroendocrine neoplasms.

Pre-assignment

Screening details:

We prospectively included 116 patients who fullfilled inclusion and exclusion criteria. Of the 116, 17 did not undergo uPAR PET/CT (worsening of disease, n=5; withdrawal of consent, n=5; death before uPAR PET/CT, n=4; impossibility of performing uPAR PET/CT because of coronavirus disease 2019 restrictions, n=3).

Pre-assignment period milestones

Number of subjects started	116
Number of subjects completed	116

Period 1

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

Blinding implementation details:

An experienced board-certified nuclear medicine physician together with an experienced board-certified radiologist analyzed side by side the PET/CT scans. The readers were masked to patient data.

Arms

Arm title	Experimental arm
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	68Ga-NOTA-AE105
Investigational medicinal product code	SUB271580 - [68Ga]Ga-NOTA-AE105
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

One injection of up to 236 MBq 68Ga-NOTA-AE105

Number of subjects in period 1	Experimental arm
Started	116
Completed	99
Not completed	17
Consent withdrawn by subject	5
worsening of disease	5

COVID 19 impossibility of performing uPAR PET/CT	3
death before uPAR PET/CT	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
All patients fullfilling the inclusion/exclusion criteria and included in the study	

Reporting group values	Overall trial	Total	
Number of subjects	116	116	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	67		
full range (min-max)	34 to 82	-	
Gender categorical Units: Subjects			
Female	49	49	
Male	67	67	

Subject analysis sets	
Subject analysis set title	Primary analysis set
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients who underwent uPAR PET/CT and had evaluable lesions (visible lesions on PET and or CT)	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who underwent uPAR PET/CT	
Subject analysis set title	Secondary analyses set - low uPAR
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients were dicotomized by tumor uPAR uptake in a group of low and high uptake	
Subject analysis set title	Secondary analyses set - high uPAR
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients were dicotomized (by median) by their tumor uPAR uptake in low and high uptake	

Reporting group values	Primary analysis set	Safety set	Secondary analyses set - low uPAR
Number of subjects	96	99	48
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	66	66	63
full range (min-max)	34 to 82	34 to 82	48 to 78
Gender categorical			
Units: Subjects			
Female	39	41	20
Male	57	58	28

Reporting group values	Secondary analyses set - high uPAR		
Number of subjects	48		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	70		
full range (min-max)	34 to 82		
Gender categorical			
Units: Subjects			
Female	19		
Male	29		

End points

End points reporting groups

Reporting group title	Experimental arm
Reporting group description: -	
Subject analysis set title	Primary analysis set
Subject analysis set type	Per protocol
Subject analysis set description: All patients who underwent uPAR PET/CT and had evaluable lesions (visible lesions on PET and or CT)	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who underwent uPAR PET/CT	
Subject analysis set title	Secondary analyses set - low uPAR
Subject analysis set type	Per protocol
Subject analysis set description: Patients were dicotomized by tumor uPAR uptake in a group of low and high uptake	
Subject analysis set title	Secondary analyses set - high uPAR
Subject analysis set type	Per protocol
Subject analysis set description: Patients were dicotomized (by median) by their tumor uPAR uptake in low and high uptake	

Primary: uPAR PET-positive tumors

End point title	uPAR PET-positive tumors[1]
End point description:	
End point type	Primary
End point timeframe: Assessed following the performance of uPAR PET	

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 analysis of the number of patients with uPAR positive lesions

End point values	Primary analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	96			
Units: number of patients				
Positive	65			
Negative	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

End point type	Secondary

End point timeframe:

During at least 1 year follow-up after uPAR PET/CT

End point values	Primary analysis set	Secondary analyses set - low uPAR	Secondary analyses set - high uPAR	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	96	48	48	
Units: number of patients				
Progressive disease	59	23	36	
Non-progressive disease	37	25	12	

Statistical analyses

Statistical analysis title	Cox regression analysis
Comparison groups	Secondary analyses set - low uPAR v Secondary analyses set - high uPAR
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	3.17

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

At least one year follow-up after uPAR PET/CT

End point values	Primary analysis set	Secondary analyses set - low uPAR	Secondary analyses set - high uPAR	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	96	48	48	
Units: number of patients				
Dead	28	9	19	
Alive	68	39	29	

Statistical analyses

Statistical analysis title	Cox regression analysis
Comparison groups	Secondary analyses set - low uPAR v Secondary analyses set - high uPAR
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	5.88

Notes:

[2] - Patients were dichotomized by median values

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Within 24 hours of uPAR PET/CT	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	5
Reporting groups	
Reporting group title	All patients scanned
Reporting group description: All patients who underwent uPAR PET/CT	

Serious adverse events	All patients scanned		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 99 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	All patients scanned		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 99 (1.01%)		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2018	New principal investigator

Notes:

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/35058319