Clinical trial results:
Patterns of uptake of 18F-FDG and 68Ga-DOTA PET in advanced neuroendocrine tumors

Summary

EudraCT number	2018-000398-64
Trial protocol	ES
Global end of trial date	02 December 2019

Results information

Result version number	v1 (current)
This version publication date	04 June 2022
First version publication date	04 June 2022
Summary attachment (see zip file)	DOTATOC Final study report (CSR_DOTATOC_Final_1.0_15June2021_FE.pdf)

Trial information

Trial identification

Sponsor protocol code	VHIO18001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VHIO
Sponsor organisation address	Carrer de Natzaret, 117, 08035 Barcelona, España, Barcelona, Spain, 08035
Public contact	Clinical Research Support Unit, Vall d' Hebron Institute of Oncology (VHIO), 34 932 543 4508614, smunoz@vhio.net
Scientific contact	Clinical Research Support Unit, Vall d' Hebron Institute of Oncology (VHIO), 605925779 932 543 4508614, smunoz@vhio.net

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 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 June 2019
Global end of trial reached?	Yes
Global end of trial date	02 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1-To determine the sensitivity of 68Ga-DOTA PET-CT to detect tumors with high expression of RSST as compared to that of standard of care with octreotide labeled with gamma-emitting radionuclides
2- To identify the uptake patterns of 18F-FDG and 68Ga-DOTA PET-CT within subjects with well or moderately differentiated metastatic GEP-NET (ENETS grades 1 and 2).
3-To establish the correlation between the functional characteristics of hepatic lesions and the level of uptake of 18F-FDG and 68Ga.
4-To explore the impact of this combined imaging test on therapeutics.

Protection of trial subjects:

Two days after injection of the radiotracer 68Ga-DOTATOC, a follow-up phone call was carried out to ask for and assess any experienced adverse events.
No immediate adverse reaction related to radiotracer injection was reported and the subjects reported no adverse events from the time of radioisotope injection until two days after the imaging probe.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2018
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	Spain: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	22
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were diagnosed using a routine diagnostic algorithm. This includes routine imaging tests (CT, MRI, PET-FDG) to locate and characterize the primary tumor as well as a scintigraphy with receptors of the somatostatin to determine the affinity of the tumor to the analogs. The oncologist recruited the patients and perform a clinic visit.

Pre-assignment

Screening details:

The study population were composed of 30 patients with metastatic NET. Inclusion criteria:
1. Patients older than 18 years.
2. Grade 1 and 2 NETs according to WHO and ENETS classification.
3. Metastatic NETs.
4. Life expectancy > 12 months.
5. Signed written informed consent

Period 1

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

Arms

Arm title	Complete Set

Arm description:

In this study there is only 1 arm

Arm type	Experimental
Investigational medicinal product name	SomaKit TOC (edotreotide or DOTATOC)
Investigational medicinal product code	SUB183602
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The recommended activity for an adult weighing 70 kg is 100 to 200 MBq, administered by direct slow intravenous injection.
The activity will be adapted to the characteristics of the patient, the type of PET camera used and the mode of acquisition.
The Reaction Buffer vial contains approximately 32.5 mg of sodium.

Number of subjects in period 1	Complete Set
Started	30
Completed	30

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	30	30	
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)	22	22	
From 65-84 years	8	8	
85 years and over	0	0	
Adults	0	0	
Older	0	0	
Age continuous Units: years			
median	58.1		
full range (min-max)	36 to 82	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	11	11	

End points

End points reporting groups	
Reporting group title	Complete Set
Reporting group description: In this study there is only 1 arm	
Subject analysis set title	68Ga-DOTATOC PET/CT
Subject analysis set type	Full analysis
Subject analysis set description: All patients undergoing 68Ga-DOTATOC PET/CT	
Subject analysis set title	99mTc-Tektrotyd SPECT
Subject analysis set type	Full analysis
Subject analysis set description: All patients undergoing 99mTc-Tektrotyd SPECT	
Subject analysis set title	18F-FDG PET/CT
Subject analysis set type	Full analysis
Subject analysis set description: All patients undergoing 18F-FDG PET/CT	

Primary: Sensitivity of 68Ga-DOTATOC PET/CT vs 99mTc-Tektrotyd SPECT	
End point title	Sensitivity of 68Ga-DOTATOC PET/CT vs 99mTc-Tektrotyd SPECT
End point description: The performance of both imaging methods was analyzed and compared for the detection of primary tumor, loco-regional tumor (N1) and global tumor lesions (M1). A region was regarded positive if at least 1 lesion was detected in that region. Additionally, number of detected lesions were also compared between both methods according to the location and involved organs as follows: 1) liver, 2) lung, 3) bone, 4) nodal infra, 5) nodal supra and 6) soft tissues of the body.	
End point type	Primary
End point timeframe: This endpoint was evaluated after having performed both tests in each of the patients included in the trial	

End point values	68Ga-DOTATOC PET/CT	99mTc-Tektrotyd SPECT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Sensitivity (%)				
number (not applicable)				
Primary tumour	39.3	39.3		
Loco-regional tumour (N1)	63.3	43.3		
Global tumour lesions (M1)	100	90		

Attachments (see zip file)	Sensitivity (number of lesions)/Primary (number of lesions).pdf

Statistical analyses

Statistical analysis title	Sensitivity in the detection of primary tumour
Statistical analysis description:	
Differences in diagnostic performance (sensitivity) between the PET/CT and SPECT results were tested for significance using McNemar's test (two level of significance <0.05).	
Comparison groups	99mTc-Tektrotyd SPECT v 68Ga-DOTATOC PET/CT
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Mcnemar

Statistical analysis title	Sensitivity in loco-regional tumour (N1)
Statistical analysis description:	
Differences in diagnostic performance (sensitivity) between the PET/CT and SPECT results were tested for significance using McNemar's test (two level of significance <0.05).	
Comparison groups	68Ga-DOTATOC PET/CT v 99mTc-Tektrotyd SPECT
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.034
Method	Mcnemar

Statistical analysis title	Sensitivity in global tumour lesions (M1)
Statistical analysis description:	
Differences in diagnostic performance (sensitivity) between the PET/CT and SPECT results were tested for significance using McNemar's test (two level of significance <0.05).	
Comparison groups	99mTc-Tektrotyd SPECT v 68Ga-DOTATOC PET/CT
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.083
Method	Mcnemar

Primary: Sensitivity of 68Ga-DOTATOC PET/CT vs 18F-FDG PET/CT

End point title	Sensitivity of 68Ga-DOTATOC PET/CT vs 18F-FDG PET/CT
End point description:	
The performance of both imaging methods was analyzed and compared for the detection of primary tumor, loco-regional tumor (N1) and global tumor lesions (M1). A region was regarded positive if at least 1 lesion was detected in that region. Additionally, number of detected lesions were also compared between both methods according to the location and involved organs as follows: 1) liver, 2) lung, 3) bone, 4) nodal infra, 5) nodal supra and 6) soft tissues of the body.	
End point type	Primary
End point timeframe:	
This endpoint was evaluated after having performed both tests in each of the patients included in the	

trial.

End point values	68Ga-DOTATOC PET/CT	18F-FDG PET/CT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Sensitivity (%)				
number (not applicable)				
Primary tumour	37.9	31.0		
Loco-regional tumor (N1)	63.3	31.6		
Global tumour (M1)	100	66.7		

Attachments (see zip file)	Sensitivity (number of lesions)/Primary (number of lesions)_2.

Statistical analyses

Statistical analysis title	Sensitivity in primary tumour
Statistical analysis description:	
Differences in diagnostic performance (sensitivity) between the PET/CT and SPECT results were tested for significance using McNemar's test (two level of significance <0.05).	
Comparison groups	68Ga-DOTATOC PET/CT v 18F-FDG PET/CT
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.317
Method	Mcnemar

Statistical analysis title	Sensitivity in loco-regional tumour (N1)
Statistical analysis description:	
Differences in diagnostic performance (sensitivity) between the PET/CT and SPECT results were tested for significance using McNemar's test (two level of significance <0.05).	
Comparison groups	68Ga-DOTATOC PET/CT v 18F-FDG PET/CT
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mcnemar

Statistical analysis title	Sensitivity in global tumour (M1)
Statistical analysis description:	
Differences in diagnostic performance (sensitivity) between the PET/CT and SPECT results were tested	

for significance using McNemar’s test (two level of significance <0.05).

Comparison groups	68Ga-DOTATOC PET/CT v 18F-FDG PET/CT
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mcnemar

Secondary: Change in therapeutic decision

End point title	Change in therapeutic decision

End point description:

The impact of additional data provided by 68Ga-DOTATOC PET/CT on the patient’s management was assessed.

End point type	Secondary

End point timeframe:

This endpoint was evaluated after having performed study tests in each of the patients included in the trial.

End point values	Complete Set			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage				
number (not applicable)	67.7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All patients were followed for safety two days after the 68Ga-DOTATOC PET/CT scan was performed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Safety analysis set

Reporting group description:

The safety analysis set was defined as all patients who underwent 68Ga -DOTATOC PET/CT.

Serious adverse events	Safety analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (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	Safety analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		

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: There were no serious adverse events reported in this study

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