Clinical trial results:
A Phase II, Open Label, Uncontrolled and Multicenter Trial of Pazopanib Given as a Single Agent in Patients With Progressive Advanced/Metastatic Neuroendocrine Tumors (NET)

Summary

EudraCT number	2010-020749-28
Trial protocol	ES
Global end of trial date	15 March 2017

Results information

Result version number	v1 (current)
This version publication date	27 November 2021
First version publication date	27 November 2021
Summary attachment (see zip file)	GETNE 1002 Final Manuscript (GETNE 1002 AnnalsofOncology.pdf)

Trial information

Trial identification

Sponsor protocol code	GETNE-1002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01280201
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GETNE
Sponsor organisation address	Velázquez, 7, 3ª planta, Madrid, Spain, 28001
Public contact	GETNE Technical Secretariat, GETNE Technical Secretariat, getne@getne.org
Scientific contact	GETNE Technical Secretariat, GETNE Technical Secretariat, getne@getne.org

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	12 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2015
Global end of trial reached?	Yes
Global end of trial date	15 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to determine the clinical benefit rate at 6 months. Clinical benefit is defined as the percentage of patients with complete response + partial response + stable disease. Efficacy will be determined according to RECIST V 1.0

Protection of trial subjects:

The study was approved by an independent ethics committee according to local laws and complied with the International Conference on Harmonization Good Clinical Practice guidelines and the Declaration of Helsinki. All patients granted informed consent in writing before study entry.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2011
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: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	27
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Open labelled and competitive recruitment. Confirmed pathological diagnosis of moderately to well-differentiated metastatic or locally advanced pancreatic islet cell tumors, gastrointestinal, bronchial or thymic NETs, not candidates for surgery, at least one measurable target lesion, ECOG 0-1,and adequate hematological, hepatic and renal function.

Pre-assignment

Screening details:

Confirmed pathological diagnosis of moderately to well-differentiated metastatic or locally advanced pancreatic islet cell tumors, gastrointestinal, bronchial or thymic NETs, not candidates for surgery, at least one measurable target lesion, ECOG 0-1,and adequate hematological, hepatic and renal function.

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	Pazopanib

Arm description:

Single arm of pazopanib 800 mg (2x400mg) given once daily as a single agent.

Arm type	Experimental
Investigational medicinal product name	Pazopanib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

The patients received oral pazopanib 800 mg/day during a 28-day treatment cycle. They were allowed to receive concomitant treatment with somatostatin analogs at the investigator’s discretion. Pazopanib dose reductions were allowed as follows: level 1: 600 mg and level 2: 400 mg. Study therapy was discontinued when clinical or radiological evidence of progressive disease was documented, when a participant experienced unacceptable adverse events (AEs), withdrew consent or per investigator’s decision.

Number of subjects in period 1	Pazopanib
Started	44
Completed	44

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	44	44	
Age categorical			
Eligible patients were aged ≥18 years			
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)	27	27	
From 65-84 years	17	17	
85 years and over	0	0	
Age continuous			
Units: years			
median	60.2		
standard deviation	± 10.9	-	
Gender categorical			
Units: Subjects			
Female	20	20	
Male	24	24	

Subject analysis sets	
Subject analysis set title	Intention to treat
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients participating in the study.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

Patients registered and have computed tomographic scan for tumor response evaluation

Reporting group values	Intention to treat	Per Protocol	
Number of subjects	44	42	
Age categorical			
Eligible patients were aged ≥18 years			
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)	27	27	
From 65-84 years	17	15	
85 years and over	0	0	
Age continuous			
Units: years			
median	60.2	59.7	
standard deviation	± 10.9	± 10.5	
Gender categorical			
Units: Subjects			
Female	20	20	
Male	24	22	

End points

End points reporting groups

Reporting group title	Pazopanib
Reporting group description:	
Single arm of pazopanib 800 mg (2x400mg) given once daily as a single agent.	
Subject analysis set title	Intention to treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients participating in the study.	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients registered and have computed tomographic scan for tumor response evaluation	

Primary: Clinical Benefit Rate

End point title	Clinical Benefit Rate
End point description:	
Per Response Evaluation Criteria In Solid Tumor Criteria (RECIST v1.0) for target lesions and assessed by MRI: complete response (CR) considered as dissapereance of all target lesions: partial response (PR), considered as >=30% decrease in the sum of the longest diameter of target lesions, or stable disease (SD) considered as a decrease <30%, after pazopanib was started. Clinical benefit rate (CBR) was defined as the percentage of patients achieving CR, PR or SD.	
End point type	Primary
End point timeframe:	
6 months	

End point values	Pazopanib	Per Protocol		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	42	42		
Units: patients	25	25		

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Pazopanib v Per Protocol
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	percentage of patients
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.7

Notes:

[1] - Descrptive statistics.

Secondary: Number of Patients Who Had an Event (Disease Progression or Death)

End point title	Number of Patients Who Had an Event (Disease Progression or Death)

End point description:

Per Response Evaluation Criteria In Solid Tumor Criteria (RECIST v1.0) for target lesions and assessed by MRI, considered as the proportion of patietnts whose target lesions have been reported with a >=30% increase in the sum of the longest diameter of target lesions.

End point type	Secondary

End point timeframe:

3 years

End point values	Pazopanib	Intention to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	40	40		
Units: Patients	35	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Radiological Objective Complete Response Rate

End point title	Radiological Objective Complete Response Rate

End point description:

Per Response Evaluation Criteria In Solid Tumor Criteria (RECIST v1.0) for target lesions and assessed by MRI, considered as the proportion of patients whose target lessions have dissaperead after treatment.

End point type	Secondary

End point timeframe:

3 years

End point values	Pazopanib	Intention to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	44		
Units: Patient	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

Defined, for the subset of patients with a confirmed CR o PR, as the time from first documented evidence of CR or PR until first documented disease progression or death due to any cause. The DR data will be censored the day after the last evaluation in those patients who did not present an objective tumoral progression and did not died during their participation in the trial. The DR will be assessed only in the subset of patients presenting objective response.

End point type	Secondary

End point timeframe:

3 years

End point values	Pazopanib	Intention to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	44		
Units: month				
median (full range (min-max))	11.3 (2.0 to 20.6)	11.3 (2.0 to 20.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Assessment Criteria

End point title	Safety Assessment Criteria

End point description:

Number of participantes with grade 3 or 4 AEs. Safety and tolerance to the study medication will be determined evaluating the type, incidence, severity, timing, seriousness and connections with the treatment of the reported adverse events, physical examinations and laboratory tests. Toxicity will be classified according to NCI-CTCAE v 4.0.

End point type	Secondary

End point timeframe:

3 years

End point values	Pazopanib	Intention to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	44		
Units: adverse events	28	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Predictive Value of Baseline CTC (Count of 0) for Response

End point title	Predictive Value of Baseline CTC (Count of 0) for Response

End point description:

Predictive value of the differente biomarkers included in the study was evaluated using multivariate analysis.

End point type	Secondary

End point timeframe:

3 years

End point values	Pazopanib	Intention to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	44		
Units: Odds ratio				
number (confidence interval 95%)	6.2 (0.45 to 86.5)	6.2 (0.45 to 86.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

4 years, 8 months

Assessment type	Systematic

Dictionary used

Dictionary name	CTC AE
Dictionary version	4.0

Reporting groups

Reporting group title	Pazopanib

Reporting group description:

Single arm of pazopanib 800 mg (2x400mg) given once daily as a single agent.

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: Table 2 of the manuscript publicated of the study DOI:https://doi.org/10.1093/annonc/mdv252, provides the summary of adverse events occurring in more than 10% of the subjects. The manuscript if freely open for any individual.

Serious adverse events	Pazopanib		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 44 (43.18%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMORAL PAIN			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive crisis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CEREBELLOUS HEMATOMA			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
DISSEMINATED INTRAVASCULAR COAGULATION				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Abdominal pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PROGRESSION DISEASE				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
GENERALIZED CRISIS				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
INJURY IN HYPOPHYSIS				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				

Acute coronary syndrome				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
intestinal suboclussion				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	2 / 44 (4.55%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
INTESTINAL BLEEDING				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatotoxicity				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
OBSTRUCTIVE ICTERY				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ALT AND AST INCREASE				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hepatic encephalopathy				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
BILIARY STENOSIS				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERTRANSAMINASEMIA				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

LIVER FAILURE				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Cellulitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
RENAL INSUFFICIENCY				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
DIABETIC DECOMPENSATION				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
OLIGOARTRALGIAS				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
RESPIRATORY INFECTION BY E.COLI				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ACTIVE TUBERCULOSIS			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
HYPERGLUCEMIA			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COMA HYPOGLYCEMIC			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Pazopanib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 44 (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

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

Small sample size, heterogeneous location and degree of differentiation of primary tumors, and lack of an appropriate control group. Additionally,response was evaluated by the investigator and not by an independent committee.

Notes: