



Clinical trial results:

Phase II study to evaluate efficacy of rechallenge with Sunitinib in Patients with Metastatic Pancreatic Neuroendocrine Tumor (pNETs) well differentiated G1/2 advanced or metastatic who previously failed to sunitinib (The RESUNET Trial)

Summary

EudraCT number	2015-005774-37
Trial protocol	ES
Global end of trial date	23 October 2019

Results information

Result version number	v1 (current)
This version publication date	02 June 2021
First version publication date	02 June 2021

Trial information

Trial identification

Sponsor protocol code	GETNE-2016-01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Grupo Español de Tumores Neuroendocrinos - GETNE
Sponsor organisation address	Calle Balmes 243, Escalera A, 5º1a, Barcelona, Spain, 08006
Public contact	Secretaría Técnica GETNE, Grupo Español de Tumores Neuroendocrinos - GETNE, +34 93 434 44 12,
Scientific contact	Secretaría Técnica GETNE, Grupo Español de Tumores Neuroendocrinos - GETNE, +34 93 434 44 12,

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	16 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 October 2019
Global end of trial reached?	Yes
Global end of trial date	23 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate sunitinib efficacy in Patients with Metastatic Pancreatic Neuroendocrine Tumor (pNETs) well differentiated G1/2 advanced or metastatic who previously failed to sunitinib

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 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	Spain: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited in the study from 14th february 2017 until 29th may 2019

Pre-assignment

Screening details:

Patients with an advanced or metastatic G1/G2 pancreatic neuroendocrine tumour who have failed treatment with sunitinib for advanced disease and who have received at least one other line of systemic treatment with everolimus.

Period 1

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

Arms

Arm title	Study treatment
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Arm description:

Patients received sunitinib 37.5 mg daily administered continuously in 28-day cycles. Co-administration with supportive therapies such as somatostatin analogues to control hypersecretory syndrome secondary to the tumour disease itself was permitted during study treatment. Treatment with sunitinib was maintained until confirmation of tumour progression according to RECIST v1.1 criteria.

Arm type	Experimental
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

37.5 mg daily in 28-day cycles until disease progression.

Number of subjects in period 1	Study treatment
Started	11
Completed	11

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	11	11	
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	5	5	
85 years and over	0	0	
Age continuous			
Units: years			
median	55.0		
full range (min-max)	36.0 to 75.0	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	4	4	
Race			
Units: Subjects			
Caucasian	11	11	
ECOG-PS			
Units: Subjects			
ECOG-PS 0	5	5	
ECOG-PS 1	6	6	
TNE Grade			
Units: Subjects			
G1	1	1	
G2	9	9	
G3	1	1	
Number of location per patient			
Units: Subjects			
One	4	4	
Two	6	6	
Three	1	1	
TNM: Stage at initial diagnosis			
Units: Subjects			
IIA	1	1	

IIB	1	1	
IV	9	9	
Octreoscan Evaluation Units: Subjects			
Not performed	6	6	
Performed (Positive result)	5	5	
Previous treatments: Targeted therapies Units: Subjects			
Yes	11	11	
No	0	0	
Previous targeted therapies: Sunitinib Units: Subjects			
Yes	11	11	
No	0	0	
Previous targeted therapies: Everolimus Units: Subjects			
Yes	10	10	
No	1	1	
Previous targeted therapies: Others Units: Subjects			
Tremelimumab + Durvalumab	2	2	
Lenvatinib	1	1	
Palbociclib	1	1	
Sandostatin	1	1	
Somatuline autogel	1	1	
No	5	5	
Previous treatments: Surgery Units: Subjects			
Yes	9	9	
No	2	2	
Previous treatments: Radiotherapy Units: Subjects			
Yes	0	0	
No	11	11	
Previous treatments: locoregional therapy			
The patient was treated with selective hepatic chemoembolization.			
Units: Subjects			
Yes	1	1	
No	10	10	
Previous chemotherapy: Temozolomide + Capecitabine Units: Subjects			
Yes	3	3	
No	8	8	
Previous chemotherapy: Platine + Etoposide Units: Subjects			
Yes	3	3	
No	8	8	
Previous chemotherapy: Estreptozocine + 5-FU			

Units: Subjects			
Yes	2	2	
No	9	9	
Previous chemotherapy: Lurbinectidine			
Units: Subjects			
Yes	2	2	
No	9	9	
Tumor location: Liver			
Units: Subjects			
Yes	10	10	
No	1	1	
Tumor location: Lymph nodes			
Units: Subjects			
Yes	4	4	
No	7	7	
Tumor location: Pancreas			
Units: Subjects			
Yes	2	2	
No	9	9	
Tumor location: Lungs			
Units: Subjects			
Yes	2	2	
No	9	9	
Weight			
Units: Kg			
median	61.5		
full range (min-max)	45.6 to 83.2	-	
Height			
Units: Cm			
median	165.0		
full range (min-max)	145.0 to 179.0	-	
Time since first diagnosis			
Time elapsed in months from date of initial diagnosis to date of patient informed consent.			
Units: Months			
median	58.1		
full range (min-max)	21.6 to 143.7	-	
Time since advanced or metastatic disease			
Time elapsed in months from the date of diagnosis of advanced or metastatic disease to the date of the patient's informed consent.			
Units: Months			
median	58.1		
full range (min-max)	21.6 to 120.0	-	
Mitotic index: Ki67			
Units: Percentage (%)			
median	15.0		
full range (min-max)	5.0 to 37.0	-	
Tumor size			
Units: Mm			
median	33.5		
full range (min-max)	22.0 to 110.0	-	
Treatment duration			

Time elapsed in weeks from the date on which the patient receives the first dose of treatment to the date of withdrawal of treatment.			
Units: Weeks			
median	22.6		
full range (min-max)	8.0 to 69.0	-	
Dose intensity			
Amount of Study drug that the patient receives.			
Units: Mg/week			
median	246.6		
full range (min-max)	169.6 to 262.5	-	
Relative dose intensity			
Amount of Study drug that the patient receives in relation to the amount of study drug he/she should receive according to the protocol.			
Units: Percentage (%)			
median	94		
full range (min-max)	65 to 100	-	

End points

End points reporting groups

Reporting group title	Study treatment
Reporting group description: Patients received sunitinib 37.5 mg daily administered continuously in 28-day cycles. Co-administration with supportive therapies such as somatostatin analogues to control hypersecretory syndrome secondary to the tumour disease itself was permitted during study treatment. Treatment with sunitinib was maintained until confirmation of tumour progression according to RECIST v1.1 criteria.	

Primary: 6 months progression free survival

End point title	6 months progression free survival ^[1]
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End point description:

End point type	Primary
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End point timeframe:

Since start of treatment until radiological evidence of disease progression.

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: One arm non-controlled clinical trial. Only descriptive analyses performed. No comparisons.

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage (%)				
number (confidence interval 95%)	62.3 (33.7 to 90.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate

End point title	Overall response rate
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End point description:

1 of 11 patients show partial response (9.1%)

End point type	Secondary
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End point timeframe:

Since start of treatment until disease progression, unacceptable toxicity or investigator decision.

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage (%)				
number (confidence interval 95%)	9.1 (0.0 to 26.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical benefit

End point title	Clinical benefit
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End point description:

Clinical benefit: Complete response + partial response + stable disease.

1 patient experienced partial response. 7 patients experienced stable disease. The amount of both is 8 from 11 patients (72,7%).

End point type	Secondary
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End point timeframe:

Since start of treatment until disease progression, unacceptable toxicity or investigator decision.

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage (%)				
number (confidence interval 95%)	72.7 (46.4 to 99.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment until end of treatment.

Adverse event reporting additional description:

The analysis of adverse events was performed for total number of patients who received at least one dose of sunitinib.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Study treatment
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Reporting group description: -

Serious adverse events	Study treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Deterioration of general condition	Additional description: Deterioration of general condition Grade 3		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia	Additional description: Pyrexia Grade 2		
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Study treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Surgical and medical procedures			

Hypertension subjects affected / exposed occurrences (all)	Additional description: 1 Hypertension Grade 1 and 1 Grade 2.		
	2 / 11 (18.18%) 2		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Face oedema subjects affected / exposed occurrences (all) Mucosal inflammation subjects affected / exposed occurrences (all) Xerosis subjects affected / exposed occurrences (all)	Additional description: 4 Asthenia Grade 1 and 3 Grade 2.		
	7 / 11 (63.64%) 7		
	Additional description: Face oedema Grade unknown		
	1 / 11 (9.09%) 1		
	Additional description: Mucosal inflammation Grade 1		
	1 / 11 (9.09%) 1		
	Additional description: Xerosis Grade 2		
	1 / 11 (9.09%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	Additional description: Dyspnoea Grade 3.		
	1 / 11 (9.09%) 1		
Investigations Transaminases increased subjects affected / exposed occurrences (all)	Additional description: Transaminases increased Grade 1		
	1 / 11 (9.09%) 1		
Cardiac disorders Congestive cardiac failure subjects affected / exposed occurrences (all)	Additional description: Congestive cardiac failure grade 2		
	1 / 11 (9.09%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all)	Additional description: Headache Grade 2		
	1 / 11 (9.09%) 1		
	Additional description: 1 Dysgeusia Grade 1 and 2 Grade 2.		
	3 / 11 (27.27%) 3		
Blood and lymphatic system disorders			

Leukopenia subjects affected / exposed occurrences (all)	Additional description: Leukopenia Grade 2		
	1 / 11 (9.09%)		
	1		
Thrombocytopenia subjects affected / exposed occurrences (all)	Additional description: 1 Thrombocytopenia Grade 1 and 1 Grade 2		
	2 / 11 (18.18%)		
	2		
Neutropenia subjects affected / exposed occurrences (all)	Additional description: 1 Neutropenia Grade 1 and 2 Grade 3		
	3 / 11 (27.27%)		
	3		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	Additional description: 2 Diarrhoea Grade 1, 1 Grade 2 and 1 Grade 3.		
	4 / 11 (36.36%)		
	4		
Abdominal pain subjects affected / exposed occurrences (all)	Additional description: Abdominal pain Grade 2		
	1 / 11 (9.09%)		
	1		
Abdominal pain upper subjects affected / exposed occurrences (all)	Additional description: Abdominal pain upper Grade 1		
	1 / 11 (9.09%)		
	1		
Stomatitis subjects affected / exposed occurrences (all)	Additional description: Stomatitis Grade 3		
	1 / 11 (9.09%)		
	1		
Constipation subjects affected / exposed occurrences (all)	Additional description: Constipation Grade 2		
	1 / 11 (9.09%)		
	1		
Flatulence subjects affected / exposed occurrences (all)	Additional description: Flatulence Grade 1		
	1 / 11 (9.09%)		
	1		
Nausea subjects affected / exposed occurrences (all)	Additional description: 2 Nausea Grade 2		
	2 / 11 (18.18%)		
	2		
Vomiting subjects affected / exposed occurrences (all)	Additional description: Vomiting Grade 2		
	1 / 11 (9.09%)		
	1		
Hepatobiliary disorders			

Hypertension portal subjects affected / exposed occurrences (all)	Additional description: Hypertension portal Grade 2		
	1 / 11 (9.09%) 1		
Jaundice subjects affected / exposed occurrences (all)	Additional description: Jaundice Grade 1		
	1 / 11 (9.09%) 1		
Skin and subcutaneous tissue disorders			
Achromotrichia congenital subjects affected / exposed occurrences (all)	Additional description: Achromotrichia congenital Grade 1		
	1 / 11 (9.09%) 1		
Eruption subjects affected / exposed occurrences (all)	Additional description: Eruption Grade 1		
	1 / 11 (9.09%) 1		
Skin hypopigmentation subjects affected / exposed occurrences (all)	Additional description: Skin hypopigmentation Grade 1		
	1 / 11 (9.09%) 1		
Yellow skin subjects affected / exposed occurrences (all)	Additional description: Yellow skin Grade unknown		
	1 / 11 (9.09%) 1		
Palmar-plantar erythrodysesthesia syndrome subjects affected / exposed occurrences (all)	Additional description: 1 Palmar-plantar erythrodysesthesia syndrome Grade 1, 1 Grade 2 and 1 Grade 3		
	3 / 11 (27.27%) 3		
Renal and urinary disorders			
Urinary tract infection subjects affected / exposed occurrences (all)	Additional description: Urinary tract infection Grade 2		
	1 / 11 (9.09%) 1		
Musculoskeletal and connective tissue disorders			
Arthritis subjects affected / exposed occurrences (all)	Additional description: 1 Arthritis Grade 1 and 1 Grade 2		
	2 / 11 (18.18%) 2		
Back Pain subjects affected / exposed occurrences (all)	Additional description: Back Pain Grade 1		
	1 / 11 (9.09%) 1		
Myalgia subjects affected / exposed occurrences (all)	Additional description: 1 Myalgia Grade 1 and 1 Grade 2.		
	2 / 11 (18.18%) 2		

Infections and infestations			
	Gingivitis	Additional description: Gingivitis grade 1	
	subjects affected / exposed	1 / 11 (9.09%)	
	occurrences (all)	1	
	Respiratory tract infection	Additional description: Respiratory tract infection grade 2	
	subjects affected / exposed	1 / 11 (9.09%)	
Metabolism and nutrition disorders	occurrences (all)	1	
	Tooth infection	Additional description: Tooth infection Grade 2	
	subjects affected / exposed	1 / 11 (9.09%)	
	occurrences (all)	1	
	Hypercalcemia	Additional description: Hypercalcemia Grade 3	
	subjects affected / exposed	1 / 11 (9.09%)	
	occurrences (all)	1	
	Hyperkalaemia	Additional description: Hyperkalaemia Grade 1	
	subjects affected / exposed	1 / 11 (9.09%)	
	occurrences (all)	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2016	Selection criteria updated
13 February 2017	Selection criteria updated

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.

Estimated sample size was not reached, which may affect the accuracy of the study results. Not controlled study design.

Notes: