



Clinical trial results:

A Prospective Phase II Single-Arm Trial on Neoadjuvant Peptide Receptor Radionuclide Therapy with ¹⁷⁷Lu-DOTATATE Followed by Surgery for resectable Pancreatic Neuroendocrine Tumors (Neo.Lu.Pa.NET)

Summary

EudraCT number	2019-002196-34
Trial protocol	IT
Global end of trial date	31 August 2023

Results information

Result version number	v1 (current)
This version publication date	06 June 2026
First version publication date	06 June 2026
Summary attachment (see zip file)	Neolupanet scientific article (Neolupanet Article.pdf)

Trial information

Trial identification

Sponsor protocol code	Neo.Lu.Pa.NET
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04385992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina 60, Milano, Italy, 20132
Public contact	Pancreatic surgery Unit, IRCCS Ospedale San Raffaele, partelli.stefano@hsr.it
Scientific contact	Pancreatic surgery Unit, IRCCS Ospedale San Raffaele, partelli.stefano@hsr.it

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	05 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main aim of this study is to evaluate the safety of neoadjuvant PRRT with ¹⁷⁷Lu-DOTATATE followed by surgical resection for resectable non-functioning PanNETs at high risk of recurrence.

Protection of trial subjects:

During the administration of the therapy, performed into a dedicated room of the Nuclear Medicine Division, the Health Physics staff will monitor the patient by means of an ionization chamber, in order to check the completeness of the radiopeptide administration.

In order to obtain an adequate hydration of the patient and to protect the renal parenchyma during the phase of excretion of the radiopharmaceutical from an excessive tubular reuptake of radiopetide, the administration of the radiopharmaceutical will be preceded and followed (without interruption) with intravenous infusion of 1000 ml of 0.9% sodium chloride solution containing L-Arginine hydrochloride and/or Lysine.

Patients will also be recommended to perform frequent urination (especially during the first 6 hours following the infusion of the radiopharmaceutical) to reduce the dose absorbed in the bladder and gonads.

All prophylactic and therapeutic measures will be taken to prevent and control any complications due to massive disposal of biologically active substances during or immediately after treatment, such as the administration of steroids and/or antihistamines.

Patients will be hospitalized for at least 24 hours after the administration of ¹⁷⁷Lu-DOTATATE and their discharge will be carried out in compliance with the constraints and radiation dose limits for family members and the population, according with the current Italian regulations (D.L 26 maggio 2000, n. 187). Moreover, each patient enrolled for PRRT will be given oral and written information about the rules of behaviour to be followed during the hospitalization and in the days following the discharge.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2020
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	Italy: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	23
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

31 patients were recruited in Italy (Milan, Bologna, Pisa, Peschiera del Garda, Verona) between 2020 and 2021.

Pre-assignment

Screening details:

All the patients should have performed at initial diagnosis the following procedures:

- o Thorax/abdomen CT scan with and without contrast enhancement

- o 68Gallium PET/CT or PET/MRI

- o Endoscopic ultra-sound with fine-needle aspiration/biopsy

To be enrol in the study, all the patients should have a cytological/histological confirmation of PanNET.

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	177Lu-DOTATATE
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Arm description:

Enrolled patients will be treated with standard pancreatic resection according to PanNET localization, after a course (4 cycles) of neoadjuvant PRRT with 177Lu-DOTATATE.

Arm type	Experimental
Investigational medicinal product name	177Lu-DOTATATE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection, Injection
Routes of administration	Injection , Intravenous use

Dosage and administration details:

Patients will receive a cumulative activity of 29.600 MBq (800 mCi), divided in 4 administrations (or cycles) of 7.400 MBq (200 mCi) each, with treatment intervals of 6-8 weeks. The per-cycle activity of 177Lu-DOTATATE (and consequently the cumulative activity) might be reduced if relevant blood and renal toxicity, or other side effects, will occur during the course of PRRT.

Number of subjects in period 1	177Lu-DOTATATE
Started	31
Surgical exploration	29
Completed	28
Not completed	3
Consent withdrawn by subject	2
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	31	31	
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)	23	23	
From 65-84 years	8	8	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	59		
standard deviation	± 8	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	19	19	

End points

End points reporting groups

Reporting group title	177Lu-DOTATATE
Reporting group description: Enrolled patients will be treated with standard pancreatic resection according to PanNET localization, after a course (4 cycles) of neoadjuvant PRRT with 177Lu-DOTATATE.	

Primary: Rate of postoperative 90-day morbidity and mortality

End point title	Rate of postoperative 90-day morbidity and mortality ^[1]
End point description: Rate of postoperative 90-day morbidity and mortality after neoadjuvant PRRT with 177Lu-DOTATATE followed by pancreatic resection.	
End point type	Primary
End point timeframe: From week 40 until week 52.	

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: This is a single arm trial, and to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. Given that the statistical analysis for an endpoint is not mandatory, I decided to not insert it, otherwise it gives me Error.

End point values	177Lu-DOTATATE			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Clavien Dindo scale				
number (not applicable)	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of objective radiological response to PRRT

End point title	Rate of objective radiological response to PRRT
End point description: Rate of objective radiological response to PRRT with 177Lu-DOTATATE according to modified RECIST criteria (mRECIST).	
End point type	Secondary
End point timeframe: Week 38.	

End point values	177Lu-DOTATATE			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: RECIST criteria				
number (not applicable)	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life (QoL)

End point title	Quality of life (QoL)
End point description: The quality of life (QoL) at diagnostic workup, after neoadjuvant PRRT and after the pancreatic surgical resection, will be evaluated by EORTC-QLQ-C30 questionnaire.	
End point type	Secondary
End point timeframe: Week 0, Week 38, Week 52.	

End point values	177Lu-DOTATATE			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: scores ranging from 0 to 100				
number (not applicable)	31			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Investigator is responsible for reporting all Serious Adverse Events (SAE), related or not to the study treatment, occurring during the treatment period and within 90 days of the last protocol treatment, to the "Safety Desk".

Adverse event reporting additional description:

Any late Serious Adverse Drug Reaction (SADR), occurring after the 90-day period, should follow this reporting procedure:

Fill in the SAE form and send by fax within 24 hours of the initial observation of the event, to the sponsor.

Attach a report of the event and a copy of all examinations that were carried out, including laboratory tests.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Treated group
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Reporting group description:

All patients enrolled in this study have been treated.

Serious adverse events	Treated group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Thrombocytopenia	Additional description: Mild thrombocytopenia - probable correlation with the treatment (3 doses administered) - fourth treatment suspended		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Proteinuria	Additional description: Severe - unknown relatedness to study drug - treatment suspended		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal pseudo-obstruction	Additional description: Required hospitalization - no relations with study drug, related to surgery procedure.		

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis	Additional description: Mild - no related to study drug		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Jaundice	Additional description: Mild - patient with biliary stent - no related to study drug		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis	Additional description: During postoperative period the patient developed fever with positive blood culture treated with EV antibiotics, he deleoped abdominal collection treated with replacement of abdominal drainage.		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Increased value of kidney dosimetry	Additional description: The patient performed kidney dosimetry that demonstrated a dose to the kidney of 21 Gy after 3 cycles of therapy with 177Luthathera.		
subjects affected / exposed	1 / 30 (3.33%)		
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	Treated group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)		
Blood and lymphatic system disorders			
Anemia	Additional description: RBC 2.95, Hb 8.1, HCT 26		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
addominal pain	Additional description: Moderate addominal pain		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infections and infestations			
COVID-19	Additional description: Grade 1 covid infection		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

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