Clinical trial results:
An international multi-center, open-label study to evaluate safety, tolerability, biodistribution, dosimetry and preliminary efficacy of 177Lu-OPS201 for the therapy of somatostatin receptor positive neuroendocrine tumours (NETs).

Summary

EudraCT number	2015-002867-41
Trial protocol	AT GB DK
Global end of trial date	22 February 2022

Results information

Result version number	v1 (current)
This version publication date	10 March 2023
First version publication date	10 March 2023

Trial information

Trial identification

Sponsor protocol code	OPS-C-001/D-FR-01072-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02592707
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	65, quai Georges Gorse, Boulogne Billancourt, France, 92100
Public contact	Medical Director, Ipsen Pharma, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma, clinical.trials@ipsen.com

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	22 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 February 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of peptide receptor radionuclide therapy (PRRT) with 177Lu-OPS201 administered in 3 cycles in participants with somatostatin receptor (sstr) subtype 2-positive NETs (including phaechromocytomas and paragangliomas).

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, in accordance with the International Conference on Harmonisation Consolidated Guideline on Good Clinical Practice and in compliance with Independent Ethics Committees/Institutional Review Boards and informed consent regulations.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	06 March 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	Australia: 12
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 11
Worldwide total number of subjects	40
EEA total number of subjects	17

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	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 1/2, open-label study was conducted in participants with somatostatin receptor positive NETs at 8 investigational sites between 06 March 2017 and 22 February 2022. The sponsor terminated the study early for strategic reasons and this decision was not due to any safety or tolerability concern of the study drug.

Pre-assignment

Screening details:

This was 2-part study, Part A and B. Study consisted of a screening period (up to 4 weeks), treatment period (3 core treatment cycles in Part A and B;2 additional cycles in Part B only: up to 30 months) and followed by long-term follow-up (LTFU) period (2 years). A total of 40 participants were treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A

Arm description:

Participants received 4.5 gigabecquerel (GBq) 177Lu-IPN01072 [target dose of 300 microgram (mcg) ±50 mcg] intravenous (IV) infusion on Day 1 of 3 treatment cycles. Each cycle was 8 weeks apart [+2 weeks or up to +4 weeks in case of adverse events (AE) which had not adequately recovered].

Arm type	Experimental
Investigational medicinal product name	177Lu-IPN01072
Investigational medicinal product code	
Other name	177Lu-OPS201
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 4.5 GBq of 177Lu-IPN01072 in a total volume of 20 milliliter (mL) that was administered by IV infusion over 120 minutes. The overall infusion duration did not exceeded 4 hours.

Arm title	Cohort 1: Part B

Arm description:

Participants received 6 GBq 177Lu-IPN01072 (target dose of 300 mcg) IV infusion on Day 1 of 3 treatment cycles. The radioactivity dose was reduced to 4.5 GBq in Cohort 1 adapted as recommended by data review board (DRB). As a result, Cohort 1 adapted was similar to Cohort 1 except the radioactivity dose was 4.5 GBq. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Arm type	Experimental
Investigational medicinal product name	177Lu-IPN01072
Investigational medicinal product code	
Other name	177Lu-OPS201
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 6 GBq of 177Lu-IPN01072 in a total volume of 20 mL that was administered by IV infusion over 120 minutes. The overall infusion duration did not exceeded 4 hours.

Arm title	Cohort 3: Part B

Arm description:

Participants received 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 700 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Arm type	Experimental
Investigational medicinal product name	177Lu-IPN01072
Investigational medicinal product code	
Other name	177Lu-OPS201
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 4.5 GBq of 177Lu-IPN01072 in a total volume of 20 mL that was administered by IV infusion over 120 minutes. The overall infusion duration did not exceeded 4 hours.

Arm title	Cohort 6: Part B

Arm description:

Participants received of 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 1300 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Arm type	Experimental
Investigational medicinal product name	177Lu-IPN01072
Investigational medicinal product code	
Other name	177Lu-OPS201
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 4.5 GBq of 177Lu-IPN01072 in a total volume of 20 mL that was administered by IV infusion over 120 minutes. The overall infusion duration did not exceeded 4 hours.

Number of subjects in period 1	Part A	Cohort 1: Part B	Cohort 3: Part B
Started	15	6	9
Completed	9	1	3
Not completed	6	5	6
Consent withdrawn by subject	-	1	2
Never entered LTFU period	1	-	-
Death	1	-	-
Progressive Disease	4	4	3
Unspecified	-	-	1

Number of subjects in period 1	Cohort 6: Part B
Started	10
Completed	3
Not completed	7
Consent withdrawn by subject	-
Never entered LTFU period	2

Death	-
Progressive Disease	3
Unspecified	2

Baseline characteristics

Reporting groups	
Reporting group title	Part A
Reporting group description:	
Participants received 4.5 gigabecquerel (GBq) 177Lu-IPN01072 [target dose of 300 microgram (mcg) ±50 mcg] intravenous (IV) infusion on Day 1 of 3 treatment cycles. Each cycle was 8 weeks apart [+2 weeks or up to +4 weeks in case of adverse events (AE) which had not adequately recovered].	
Reporting group title	Cohort 1: Part B
Reporting group description:	
Participants received 6 GBq 177Lu-IPN01072 (target dose of 300 mcg) IV infusion on Day 1 of 3 treatment cycles. The radioactivity dose was reduced to 4.5 GBq in Cohort 1 adapted as recommended by data review board (DRB). As a result, Cohort 1 adapted was similar to Cohort 1 except the radioactivity dose was 4.5 GBq. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).	
Reporting group title	Cohort 3: Part B
Reporting group description:	
Participants received 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 700 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).	
Reporting group title	Cohort 6: Part B
Reporting group description:	
Participants received of 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 1300 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).	

Reporting group values	Part A	Cohort 1: Part B	Cohort 3: Part B
Number of subjects	15	6	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	3	6
From 65-84 years	8	3	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	62.7	65.3	55.0
standard deviation	± 12.9	± 8.9	± 16.0
Gender categorical Units: Subjects			
Female	8	2	3
Male	7	4	6

Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	15	6	9
Other	0	0	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	15	6	9

Reporting group values	Cohort 6: Part B	Total	
Number of subjects	10	40	
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)	7	23	
From 65-84 years	3	17	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	56.7		
standard deviation	± 13.7	-	
Gender categorical Units: Subjects			
Female	6	19	
Male	4	21	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
White	9	39	
Other	0	0	
Ethnicity Units: Subjects			
Not Hispanic or Latino	10	40	

End points

End points reporting groups

Reporting group title	Part A

Reporting group description:

Participants received 4.5 gigabecquerel (GBq) 177Lu-IPN01072 [target dose of 300 microgram (mcg) ±50 mcg] intravenous (IV) infusion on Day 1 of 3 treatment cycles. Each cycle was 8 weeks apart [+2 weeks or up to +4 weeks in case of adverse events (AE) which had not adequately recovered].

Reporting group title	Cohort 1: Part B

Reporting group description:

Participants received 6 GBq 177Lu-IPN01072 (target dose of 300 mcg) IV infusion on Day 1 of 3 treatment cycles. The radioactivity dose was reduced to 4.5 GBq in Cohort 1 adapted as recommended by data review board (DRB). As a result, Cohort 1 adapted was similar to Cohort 1 except the radioactivity dose was 4.5 GBq. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Reporting group title	Cohort 3: Part B

Reporting group description:

Participants received 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 700 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Reporting group title	Cohort 6: Part B

Reporting group description:

Participants received of 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 1300 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Subject analysis set title	All Participants
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received 177Lu-IPN01072 dose from 4.5 to 6 GBq (target dose of 300 to 1300 mcg) as IV infusion on Day 1 of 3 treatment cycles/additional 2 cycles (when applicable). Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AE which had not adequately recovered).

Subject analysis set title	Part B: All Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 177Lu-IPN01072 dose from 4.5 to 6 GBq (target dose from 300 to 1300 mcg) as IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. The radioactivity dose was reduced to 4.5 GBq in Cohort 1 adapted as recommended by DRB. As a result, Cohort 1 adapted was similar to Cohort 1 except the radioactivity dose was 4.5 GBq. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs[1]

End point description:

AE is defined as any untoward medical occurrence in a subject or clinical trial subject administered a medicinal product, which did not necessarily have a causal relationship with this treatment. A serious AE (SAE) was classified as any untoward medical occurrence that at any dose results in death; AE was life threatening; required inpatient hospitalization or prolonged existing hospitalization; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect; was an important medical event that may not result in death. TEAEs are defined as AEs that developed or worsened after start of treatment. The SAS included all participants who received 177Lu-IPN01072.

End point type	Primary

End point timeframe:

From the start of the first study medication (Cycle 1 Day 1) up to 6 months after the last dose of study medication, maximum of 33 months.

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: No statistical comparisons between the treatment groups was performed for safety endpoints.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	6	9	10
Units: participants				
number (not applicable)				
TEAEs	15	6	9	10
Serious TEAEs	2	1	2	3

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: participants				
number (not applicable)				
TEAEs	40			
Serious TEAEs	8			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Dose Limiting Toxicities (DLT)

End point title	Number of Participants With Dose Limiting Toxicities (DLT)[2]

End point description:

DLTs were defined as study medication-related AEs with a severity of Grade 3 or higher are considered DLT, with the exception of hair loss, lymphopenia, nonfebrile neutropenia lasting <4 weeks and thrombocytopenia lasting <4 weeks. The SAS included all participants who received 177Lu-IPN01072.

End point type	Primary

End point timeframe:

From the start of the first study medication (Cycle 1 Day 1) up to EOCT, maximum of 16 weeks.

Notes:

[2] - 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: No statistical comparisons between the treatment groups was performed for safety endpoints.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	6	9	10
Units: participants				
number (not applicable)	3	0	2	1

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: participants				
number (not applicable)	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Uptake (%) of 177Lu-IPN01072 at Target Lesions and Discernible Organs in Cycle 1

End point title	Maximum Uptake (%) of 177Lu-IPN01072 at Target Lesions and Discernible Organs in Cycle 1

End point description:

177Lu-IPN01072 uptake in organs and lesions was evaluated centrally, using nuclear medicine images, as part of the dosimetry workflow. Uptake activity for organs of interest (i.e., body, bone marrow, kidney (left + right), healthy liver, and spleen) was determined. The maximal uptake in lesions was calculated for each lesion as: maximal activity divided injected activity*100. The Per Protocol Dosimetry Analysis set (PP-DAS) included all participants in the Intent-To-Treat Dosimetry Analysis set (ITT-DAS) for whom no major protocol violations occurred affecting dosimetry variables. Only data from the participants analyzed were reported. 99999 indicates no participants were analyzed. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycle 1

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	6	9	10
Units: percentage of injected drug activity				
median (full range (min-max))				
Bone marrow (image based) (n = 11, 6, 6, 6, 29)	0.0469 (0.0246 to 0.0751)	0.0420 (0.0100 to 0.280)	0.0250 (0.0149 to 0.0570)	0.0219 (0.0053 to 0.0300)
Liver (n = 7, 1, 0, 0, 8)	1.52 (0.314 to 6.34)	4.31 (4.31 to 4.31)	99999 (99999 to 99999)	99999 (99999 to 99999)
Kidney (left + right) (n = 11, 6, 9, 9, 35)	1.96 (0.980 to 3.82)	1.76 (1.05 to 2.08)	1.60 (1.19 to 2.51)	1.67 (0.749 to 2.41)
Spleen (n = 9, 6, 6, 6, 27)	1.50 (0.274 to 2.93)	1.27 (0.960 to 2.46)	1.78 (0.550 to 5.97)	1.79 (1.19 to 2.65)
All lesions (n = 11, 5, 9, 8, 33)	0.651 (0.0290 to 6.35)	2.36 (0.266 to 8.74)	1.18 (0.235 to 18.7)	1.43 (0.190 to 15.0)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: percentage of injected drug activity				
median (full range (min-max))				
Bone marrow (image based) (n = 11, 6, 6, 6, 29)	0.0380 (0.0053 to 0.280)			
Liver (n = 7, 1, 0, 0, 8)	2.63 (0.314 to 6.34)			
Kidney (left + right) (n = 11, 6, 9, 9, 35)	1.76 (0.749 to 3.82)			
Spleen (n = 9, 6, 6, 6, 27)	1.67 (0.274 to 5.97)			
All lesions (n = 11, 5, 9, 8, 33)	0.932 (0.0290 to 18.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximal Uptake (%) of 177Lu-IPN01072 of Blood in Cycle 1

End point title	Maximal Uptake (%) of 177Lu-IPN01072 of Blood in Cycle 1

End point description:

177Lu-IPN01072 uptake in blood was evaluated on site/locally using a gamma counter calibrated for 177Lu-IPN01072 according to the dosimetry operational manual. The radiopharmaceutical pharmacokinetic (PK) set included all participants in the ITT set who received at least 1 dose of study medication and had at least 1 measured radioactive concentration in blood. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline), 5 and 30 minutes, 1, 4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycle 1

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	8	10
Units: percentage/liter (L)				
median (full range (min-max))	3.66 (2.17 to 7.88)	2.98 (2.26 to 4.35)	2.77 (1.98 to 7.35)	3.32 (0.539 to 4.11)

End point values	All Participants			

Subject group type	Subject analysis set			
Number of subjects analysed	37			
Units: percentage/liter (L)				
median (full range (min-max))	3.03 (0.539 to 7.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve (AUC) of 177Lu-IPN01072 in Discernible Organs in Cycle 1

End point title	Area Under the Concentration Time Curve (AUC) of 177Lu-IPN01072 in Discernible Organs in Cycle 1

End point description:

The AUC of 177Lu-IPN01072 radioactivity in discernible organs were computed for each administration of 177Lu-IPN01072. The PP-DAS included all participants in the ITT-DAS for whom no major protocol violations occurred affecting dosimetry variables. Only data from the participants analyzed were reported. 99999 indicates no participants were analyzed. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycle 1

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	6	9	10
Units: Megabecquerel (MBq)*hour				
median (full range (min-max))				
Bone marrow (image based) (n = 11, 6, 6, 6, 29)	174 (45.3 to 224)	352 (154 to 3988)	138 (91.0 to 362)	157 (41.5 to 244)
Kidney (left + right) (n = 11, 6, 9, 9, 35)	9596 (3896 to 26596)	8966 (7350 to 10586)	6239 (5853 to 11269)	7578 (3320 to 9815)
Liver (n = 7, 1, 0, 0, 8)	6745 (755 to 20751)	17918 (17918 to 17918)	99999 (99999 to 99999)	99999 (99999 to 99999)
Spleen (n = 9, 6, 6, 6, 27)	6701 (1134 to 21451)	7949 (4945 to 11734)	7727 (1547 to 28269)	8179 (3901 to 12355)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: Megabecquerel (MBq)*hour				
median (full range (min-max))				
Bone marrow (image based) (n = 11, 6, 6, 6, 29)	175 (41.5 to 3988)			
Kidney (left + right) (n = 11, 6, 9, 9, 35)	8239 (3320 to 26596)			

Liver (n = 7, 1, 0, 0, 8) Spleen (n = 9, 6, 6, 6, 27)	11133 (755 to 20751) 7772 (1134 to 28269)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of 177Lu-IPN01072 in Blood in Cycle 1

End point title	AUC of 177Lu-IPN01072 in Blood in Cycle 1

End point description:

The AUC of 177Lu-IPN01072 radioactivity in blood were computed for each administration of 177Lu-IPN01072. The radiopharmaceutical PK set included all participants in the ITT set who received at least 1 dose of study medication and had at least 1 measured radioactive concentration in blood. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline), 5 and 30 minutes, 1, 4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycle 1

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	8	10
Units: MBq*hour/L				
median (full range (min-max))	623 (299 to 1003)	901 (442 to 1806)	690 (371 to 1201)	720 (290 to 1034)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	37			
Units: MBq*hour/L				
median (full range (min-max))	726 (290 to 1806)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-Life (T1/2) of Radioactivity Concentrations of the Radiopharmaceutical in Blood in Cycle 1

End point title	Terminal Half-Life (T1/2) of Radioactivity Concentrations of the Radiopharmaceutical in Blood in Cycle 1

End point description:

The terminal half-life was defined as the largest half-life of the decay curve of blood activity. The radiopharmaceutical PK set included all participants in the ITT set who received at least 1 dose of study medication and had at least 1 measured radioactive concentration in blood. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline), 5 and 30 minutes, 1, 4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycle 1

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	8	10
Units: hours				
median (full range (min-max))	68.3 (42.2 to 160)	109 (38.6 to 160)	123 (41.2 to 160)	145 (55.3 to 160)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	37			
Units: hours				
median (full range (min-max))	127 (38.6 to 160)			

Statistical analyses

No statistical analyses for this end point

Secondary: Highest Absorbed Dose of 177LU-OPS201 to Each Discernible Organ in Cycle 1

End point title	Highest Absorbed Dose of 177LU-OPS201 to Each Discernible Organ in Cycle 1

End point description:

The absorbed dose to the discernible organs (i.e., organs showing uptake) was evaluated centrally, using nuclear medicine images, as part of the dosimetry workflow. The organs considered for 177LU-OPS201 image-based dosimetry assessment included: liver, bone marrow, kidney (left + right), and spleen. The PP-DAS included all participants in the ITT-DAS for whom no major protocol violations occurred affecting dosimetry variables.

End point type	Secondary

End point timeframe:

4, 24, 48, 72 to 96 and 144 to 168 hours post infusion in Cycle 1

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: Gray				
number (not applicable)				
Bone (image-based assay)	3.59			
Kidney (left + right)	8.07			
Liver	1.26			
Spleen	8.07			

Statistical analyses

No statistical analyses for this end point

Secondary: Specific Absorbed Dose Per Organ and Lesions of 177Lu-IPN01072 in Cycle 1

End point title	Specific Absorbed Dose Per Organ and Lesions of 177Lu-IPN01072 in Cycle 1

End point description:

The specific absorbed dose was evaluated centrally, using nuclear medicine images, as part of the dosimetry workflow. Data are presented for all lesions, regardless of their anatomical localization. The organs considered for 177LUOPS201 image-based dosimetry assessment included: liver, bone marrow, kidney (left + right), and spleen. The PP-DAS included all participants in the ITT-DAS for whom no major protocol violations occurred affecting dosimetry variables. Only data from the participants analyzed were reported. 99999 indicates no participants were analyzed. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycle 1

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	6	9	10
Units: Gray/GBq				
median (full range (min-max))				
Lesions (n = 11, 5, 9, 8, 33)	2.56 (0.431 to 14.3)	3.90 (1.92 to 83.3)	6.82 (2.07 to 28.2)	13.5 (2.20 to 81.0)
Bone marrow (image based) (n = 11, 6, 6, 6, 29)	0.0796 (0.0431 to 0.216)	0.135 (0.0900 to 0.610)	0.0850 (0.0700 to 0.110)	0.0650 (0.0100 to 0.150)
Kidney (left + right) (n = 11, 6, 9, 9, 35)	1.05 (0.522 to 1.85)	0.720 (0.600 to 1.02)	0.880 (0.460 to 1.18)	0.765 (0.420 to 1.10)
Liver (n = 7, 1, 0, 0, 8)	0.186 (0.146 to 0.279)	0.170 (0.170 to 0.170)	99999 (99999 to 99999)	99999 (99999 to 99999)
Spleen (n = 9, 6, 6, 6, 27)	0.769 (0.208 to 1.79)	0.945 (0.500 to 1.08)	0.985 (0.180 to 1.46)	0.805 (0.360 to 0.980)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: Gray/GBq				
median (full range (min-max))				
Lesions (n = 11, 5, 9, 8, 33)	5.00 (0.431 to 83.3)			
Bone marrow (image based) (n = 11, 6, 6, 6, 29)	0.0900 (0.0100 to 0.610)			
Kidney (left + right) (n = 11, 6, 9, 9, 35)	0.879 (0.420 to 1.85)			
Liver (n = 7, 1, 0, 0, 8)	0.179 (0.146 to 0.279)			
Spleen (n = 9, 6, 6, 6, 27)	0.840 (0.180 to 1.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Absorbed Organ Doses of 177Lu-IPN01072 in Cycles 1 and 3

End point title	Cumulative Absorbed Organ Doses of 177Lu-IPN01072 in Cycles 1 and 3

End point description:

The cumulative absorbed dose in the discernible organs (i.e., organs showing uptake) was evaluated centrally, using nuclear medicine images, as part of the dosimetry workflow. The PP-DAS included all participants in the ITT-DAS for whom no major protocol violations occurred affecting dosimetry variables. Only data from the participants analyzed were reported. 99999 indicates no participants were analyzed. Cycle (C). Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

4, 24, 48, 72 to 96 hours, 144 to 168 hours post infusion in Cycles 1 and 3

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	6	9	10
Units: Gray				
median (full range (min-max))				
C1:Bone marrow (image based) (n = 11, 6, 6, 6, 29)	0.319 (0.102 to 0.974)	0.715 (0.390 to 3.59)	0.375 (0.260 to 0.500)	0.285 (0.0400 to 0.690)
C1:Kidney (left + right) (n = 11, 6, 9, 9, 35)	4.31 (2.17 to 8.07)	3.85 (3.36 to 4.58)	3.25 (1.79 to 5.34)	3.55 (1.74 to 4.88)
C1:Liver (n = 7, 1, 0, 0, 8)	0.720 (0.336 to 1.26)	0.810 (0.810 to 0.810)	99999 (99999 to 99999)	99999 (99999 to 99999)
C1:Spleen (n = 9, 6, 6, 6, 27)	2.88 (0.844 to 8.07)	4.35 (3.17 to 6.00)	4.00 (0.710 to 5.90)	3.55 (1.48 to 4.09)
C3:Bone marrow (image based) (n = 11, 1, 6, 3, 21)	1.11 (0.636 to 2.17)	1.48 (1.48 to 1.48)	1.09 (0.830 to 1.24)	0.840 (0.290 to 1.23)
C3:Kidney (left + right) (n = 11, 1, 8, 5, 25)	12.3 (7.67 to 24.1)	9.41 (9.41 to 9.41)	8.91 (6.29 to 14.0)	10.1 (6.95 to 11.5)

C3:Liver (n = 7, 0, 0, 0, 7)	2.08 (1.01 to 4.14)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
C3:Spleen (n = 9, 1, 5, 3, 18)	6.93 (4.99 to 15.6)	7.58 (7.58 to 7.58)	9.21 (2.82 to 14.6)	8.08 (5.66 to 14.2)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: Gray				
median (full range (min-max))				
C1:Bone marrow (image based) (n = 11, 6, 6, 6, 29)	0.400 (0.4000 to 3.59)			
C1:Kidney (left + right) (n = 11, 6, 9, 9, 35)	3.73 (1.74 to 8.07)			
C1:Liver (n = 7, 1, 0, 0, 8)	0.765 (0.336 to 1.26)			
C1:Spleen (n = 9, 6, 6, 6, 27)	3.45 (0.710 to 8.07)			
C3:Bone marrow (image based) (n = 11, 1, 6, 3, 21)	1.10 (0.290 to 2.17)			
C3:Kidney (left + right) (n = 11, 1, 8, 5, 25)	10.8 (6.29 to 24.1)			
C3:Liver (n = 7, 0, 0, 0, 7)	2.08 (1.01 to 4.14)			
C3:Spleen (n = 9, 1, 5, 3, 18)	8.32 (2.82 to 15.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Amount of Lu-177 Radioactivity Excreted Into the Urine (0 to 48 Hours) [Ae (0-48h)] in Cycle 1

End point title	Cumulative Amount of Lu-177 Radioactivity Excreted Into the Urine (0 to 48 Hours) [Ae (0-48h)] in Cycle 1

End point description:

Urine was collected during the first 48 hours post infusion to determine the renal excretion of 177Lu-IPN01072 at Cycle 1 only. The Radiopharmaceutical PK set (Part A and Part B) included all participants in the ITT set who received at least 1 dose of study medication and had at least 1 measured radioactive concentration in blood.

End point type	Secondary

End point timeframe:

0 to 6 hours, 6 to 24 hours, 24 to 48 hours post-infusion in Cycle 1 of Part A; 0 to 4 hours, 4 to 24 hours, 24 to 48 hours in Cycle 1 of Part B.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	8	9
Units: Mbq				
median (full range (min-max))	2586 (1722 to 4450)	3106 (2558 to 3998)	2640 (1346 to 3375)	2621 (471 to 3181)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: Mbq				
median (full range (min-max))	2787 (471 to 4450)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of IPN01072 in Cycle 1

End point title	Time to Reach Maximum Plasma Concentration (Tmax) of IPN01072 in Cycle 1

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion done at Cycle 1 for Part B only. The IPN01072 PK set in plasma (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and have no major protocol deviations affecting the plasma PK variables and who had a sufficient number of plasma levels to estimate the main PK parameters. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline) and 5 minutes, 30 minutes, 60 minutes, 4 hours, 6 hours, 8 hours, 24 hours, 48 hours after the end of the infusion in Cycle 1

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: hours				
median (full range (min-max))	0.083 (0.00 to 0.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of IPN01072 in Cycle 1

End point title	Maximum Observed Plasma Concentration (Cmax) of IPN01072 in Cycle 1

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion done at Cycle 1 for Part B only. The IPN01072 PK set in plasma (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and have no major protocol deviations affecting the plasma PK variables and who had a sufficient number of plasma levels to estimate the main PK parameters. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline) and 5 minutes, 30 minutes, 60 minutes, 4 hours, 6 hours, 8 hours, 24 hours, 48 hours after the end of the infusion in Cycle 1

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: nanogram (ng)/milliliter (mL)				
arithmetic mean (standard deviation)	10.7 (± 5.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC From Time Zero to Infinity (AUCinf) of IPN01072 in Cycle 1

End point title	AUC From Time Zero to Infinity (AUCinf) of IPN01072 in Cycle 1

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion done at Cycle 1 for Part B only. The IPN01072 PK set in plasma (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and have no major protocol deviations affecting the plasma PK variables and who had a sufficient number of plasma levels to estimate the main PK parameters. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline) and 5 minutes, 30 minutes, 60 minutes, 4 hours, 6 hours, 8 hours, 24 hours, 48 hours after the end of the infusion in Cycle 1

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: ng*hour (h)/mL				
arithmetic mean (standard deviation)	45.8 (± 20.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: T1/2 of IPN01072 in Cycle 1

End point title	T1/2 of IPN01072 in Cycle 1

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion done at Cycle 1 for Part B only. The IPN01072 PK set in plasma (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and have no major protocol deviations affecting the plasma PK variables and who had a sufficient number of plasma levels to estimate the main PK parameters. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline) and 5 minutes, 30 minutes, 60 minutes, 4 hours, 6 hours, 8 hours, 24 hours, 48 hours after the end of the infusion in Cycle 1

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: hours				
arithmetic mean (standard deviation)	6.09 (± 1.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Total Plasma Clearance of IPN01072 (Total CL) in Cycle 1

End point title	Apparent Total Plasma Clearance of IPN01072 (Total CL) in Cycle 1

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion done at Cycle 1 for Part B only. The IPN01072 PK set in plasma (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and have no major protocol deviations affecting the plasma PK variables and who had a sufficient number of plasma levels to estimate the main PK parameters. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline) and 5 minutes, 30 minutes, 60 minutes, 4 hours, 6 hours, 8 hours, 24 hours, 48 hours after the end of the infusion in Cycle 1

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: L/h				
arithmetic mean (standard deviation)	9.58 (± 12.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution During Terminal Phase (Vz) of IPN01072 in Cycle 1

End point title	Apparent Volume of Distribution During Terminal Phase (Vz) of IPN01072 in Cycle 1

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion done at Cycle 1 for Part B only. The IPN01072 PK set in plasma (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and have no major protocol deviations affecting the plasma PK variables and who had a sufficient number of plasma levels to estimate the main PK parameters. Only data from the participants analyzed were reported.

End point type	Secondary

End point timeframe:

Pre-infusion (Baseline) and 5 minutes, 30 minutes, 60 minutes, 4 hours, 6 hours, 8 hours, 24 hours, 48 hours after the end of the infusion in Cycle 1

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: Liter				
arithmetic mean (standard deviation)	68.7 (± 52.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ae (0-48h) of IPN01072 in Cycle 1

End point title	Ae (0-48h) of IPN01072 in Cycle 1

End point description:

Urine was collected during the first 48 hours post infusion to determine the renal excretion of 177Lu-IPN01072 at Cycle 1 for Part B only. The IPN01072 PK set in urine (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and had no major protocol deviations

affecting the urine PK variables and who had all urine IPN01072 levels available to estimate the main urine PK parameters.

End point type	Secondary

End point timeframe:

0 to 4 hours, 4 to 24 hours, 24 to 48 hours in Cycle 1 of Part B

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: mcg				
arithmetic mean (standard deviation)	141 (± 65.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Fraction of IPN01072 Excreted Into the Urine (Fe) in Cycle 1

End point title	Fraction of IPN01072 Excreted Into the Urine (Fe) in Cycle 1

End point description:

Urine was collected during the first 48 hours post infusion to determine the renal excretion of 177Lu-IPN01072 at Cycle 1 for Part B only. The IPN01072 PK set in urine (Part B only) included all participants in the ITT set who received at least 1 dose of study medication and had no major protocol deviations affecting the urine PK variables and who had all urine IPN01072 levels available to estimate the main urine PK parameters.

End point type	Secondary

End point timeframe:

0 to 4 hours, 4 to 24 hours, 24 to 48 hours in Cycle 1 in Part B

End point values	Part B: All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: percentage of drug excreted into urine				
arithmetic mean (standard deviation)	52.9 (± 24.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

The ORR was defined as the percentage of participants who achieved a complete response (CRs) or a partial response (PR) as best overall response (BOR) according centralized to response evaluation criteria in solid tumours (RECIST) version 1.1 from investigator assessment. Participants with no tumour assessment after the start of study treatment were not evaluated. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 millimeter (mm). PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. The ITT included all participants in the eligible participants set who received study medication.

End point type	Secondary

End point timeframe:

From the start of the first study medication (Cycle 1 Day 1) up to 2 years after the EOCT/death or lost to follow-up, maximum of 59 months.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	6	9	10
Units: percentage of participants				
number (confidence interval 95%)	40.0 (16.3 to 67.7)	16.7 (0.4 to 64.1)	22.2 (2.8 to 60.0)	40.0 (12.2 to 73.8)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)	32.5 (18.6 to 49.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

The DCR was defined as the percentage of participants who achieved a CR, a PR or a stable disease (SD) as BOR according to Investigator assessment RECIST version 1.1 criteria. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study. The ITT included all participants in the eligible participants set who received study medication.

End point type	Secondary

End point timeframe:

From the start of the first study medication (Cycle 1 Day 1) up to 2 years after the EOCT/death or lost to follow-up, maximum of 59 months.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	6	9	10
Units: percentage of participants				
number (confidence interval 95%)	93.3 (68.1 to 99.8)	100.0 (54.1 to 100.0)	100.0 (66.4 to 100.0)	90.0 (55.5 to 99.7)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)	95.0 (83.1 to 99.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response

End point title	Best Overall Response

End point description:

The BOR according to RECIST v1.1 was defined as the best response recorded from the initiation of treatment until the EOCT/end of additional cycles (EOAC)/early withdrawal (EW) Visit (during the core study part), prior to the Investigator assessment of progressive disease (PD). Progression was defined as at least 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this included the baseline
sum if that was the smallest on study). In addition to the relative increase of 20%, the sum also demonstrated an absolute increase of at least 5 mm.
The ITT included all participants in the eligible participants set who received study medication.

End point type	Secondary

End point timeframe:

From the start of the first study medication (Cycle 1 Day 1) up to 2 years after the EOCT/death or lost to follow-up, maximum of 59 months.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	6	9	10
Units: count of participants				
number (not applicable)				
PR	6	1	2	4
SD	8	5	7	5

PD	1	0	0	0
Not Evaluable (NE)	0	0	0	1

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: count of participants				
number (not applicable)				
PR	13			
SD	25			
PD	1			
Not Evaluable (NE)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

The PFS was defined as the time from start of study treatment until occurrence of tumour progression or death, according to Investigator assessment RECIST version 1.1. Estimation of the median was based on the Kaplan-Meier method. The ITT included all participants in the eligible participants set who received study medication. 99999 indicates upper limit of CI are non-estimable.

End point type	Secondary

End point timeframe:

From the start of the first study medication (Cycle 1 Day 1) up to 2 years after the EOCT/death or lost to follow-up, maximum of 59 months.

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	6	5
Units: months				
median (confidence interval 95%)	29.7 (17.5 to 99999)	21.2 (19.4 to 22.4)	25.1 (5.1 to 99999)	11.1 (5.1 to 99999)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: months				
median (confidence interval 95%)	28.1 (20.0 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quality of Life (QoL) Questionnaire (QLQ)-C30 at EOCT Visit

End point title	Change From Baseline in Quality of Life (QoL) Questionnaire (QLQ)-C30 at EOCT Visit

End point description:

The European Organisation for Research and Treatment of Cancer (EORTC) score QLQ-C30 was used for QoL evaluation. Each scale in the questionnaire was scored (0 to 100) according to the EORTC recommendations in the EORTC QLQ-C30 scoring manual. The scale included a global health status, where high score for the global health status represents a high QoL. The functional scales consisted of physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, where a higher value reflected a better level of function. 9 symptoms scales included nausea and vomiting, pain, fatigue, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties, where a higher value reflected worse symptoms. The ITT set. Only data from the participants analyzed were reported. 99999 indicates that standard deviation could not be calculated as only 1 participant was analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and EOCT visit (30 months)

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	1	8	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Global Health Status	1.27 (± 23.54)	16.70 (± 99999)	-6.24 (± 14.61)	29.15 (± 28.43)
Physical functioning	-2.05 (± 11.03)	0.00 (± 99999)	-0.82 (± 6.61)	10.00 (± 20.00)
Role functioning	3.85 (± 29.79)	0.00 (± 99999)	-0.01 (± 19.90)	12.50 (± 25.00)
Emotional functioning	11.52 (± 30.15)	-25.00 (± 99999)	-4.16 (± 7.74)	10.43 (± 12.51)
Cognitive functioning	6.41 (± 19.89)	0.00 (± 99999)	-6.26 (± 12.43)	12.50 (± 15.95)
Social functioning	15.38 (± 33.65)	0.00 (± 99999)	-2.09 (± 5.90)	12.50 (± 25.00)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	26			

Units: score on a scale				
arithmetic mean (standard deviation)				
Global Health Status	3.84 (± 23.83)			
Physical functioning	0.26 (± 11.70)			
Role functioning	3.85 (± 25.08)			
Emotional functioning	5.12 (± 23.70)			
Cognitive functioning	3.20 (± 17.66)			
Social functioning	8.97 (± 26.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in QLQ Gastro-intestinal. Neuroendocrine Tumour (GI.NET)21 at EOCT Visit

End point title	Change From Baseline in QLQ Gastro-intestinal. Neuroendocrine Tumour (GI.NET)21 at EOCT Visit

End point description:

The GI.NET21 module was intended for use among participants with gastrointestinal related (GI.-related) neuroendocrine tumours, who vary in disease stage and treatments. The module comprises 21 questions, consisting of 5 scales (endocrine symptoms, G.I. symptoms, treatment related symptom, social function, disease related worries) and 4 single items that assessed muscle /bone pain symptom, sexual function, information/communication function, and body image. Each question was quoted from 1 (not at all) to 4 (very much). Each scale was scored from 0 to 100. A higher value was equivalent to worse or more problems. Baseline was defined as the last non-missing measurement collected prior to the first dose of study drug (Day 1). The ITT included all participants in the eligible participants set who received study medication. Only data from the participants analyzed were reported. 99999 indicates that standard deviation could not be calculated as only 1 participant was analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and EOCT visit (30 months)

End point values	Part A	Cohort 1: Part B	Cohort 3: Part B	Cohort 6: Part B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	1	8	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Endocrine symptoms	-5.12 (± 13.31)	11.10 (± 99999)	-0.00 (± 5.93)	-5.55 (± 11.10)
G. I. symptoms	-3.58 (± 13.49)	-6.70 (± 99999)	2.50 (± 7.04)	-13.30 (± 17.22)
Treatment related symptom	5.62 (± 21.47)	-6.70 (± 99999)	9.01 (± 15.11)	-0.30 (± 8.15)
Social function	-19.67 (± 15.83)	-22.30 (± 99999)	-4.15 (± 8.29)	-30.53 (± 5.55)
Disease related worries	-8.98 (± 14.63)	-22.20 (± 99999)	3.46 (± 16.53)	-18.05 (± 13.87)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: score on a scale				
arithmetic mean (standard deviation)				
Endocrine symptoms	-2.98 (± 11.13)			
G. I. symptoms	-3.33 (± 12.81)			
Treatment related symptom	5.28 (± 17.56)			
Social function	-16.67 (± 15.17)			
Disease related worries	-7.06 (± 16.37)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of the first study medication (Cycle 1 Day 1) up to 6 months after the last dose of study medication, maximum of 33 months. Adverse events beyond 6 months after the last dose were not presented.

Adverse event reporting additional description:

The SAS included all participants who received study medication. Participants who received the therapeutic dose of 177Lu-IPN01072 during the core trial period in Part A and B.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Part A: 177Lu-IPN01072 4.5 GBq

Reporting group description:

Participants received 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg ±50 mcg) IV infusion on Day 1 of 3 treatment cycles. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AE which had not adequately recovered).

Reporting group title	Part B Cohort 1: 177Lu-IPN01072 6 GBq

Reporting group description:

Participants received 6 GBq 177Lu-IPN01072 (target dose of 300 mcg) IV infusion on Day 1 of 3 treatment cycles. The radioactivity dose was reduced to 4.5 GBq in Cohort 1 adapted as recommended by DRB. As a result, Cohort 1 adapted was similar to Cohort 1 except the radioactivity dose was 4.5 GBq. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Reporting group title	Part B Cohort 3: 177Lu-IPN01072 4.5 GBq

Reporting group description:

Participants received 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 700 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Reporting group title	Part B Cohort 6: 177Lu-IPN01072 4.5 GBq

Reporting group description:

Participants received of 4.5 GBq 177Lu-IPN01072 (target dose of 300 mcg in Cycle 1; 1300 mcg in Cycle 2; 300 mcg in Cycle 3) IV infusion on Day 1 of 3 treatment cycles. Target dose was 300 mcg for additional cycles, if any. Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AEs which had not adequately recovered).

Reporting group title	All Participants

Reporting group description:

Participants who received 177Lu-IPN01072 dose from 4.5 to 6 GBq (target dose of 300 to 1300 mcg) as IV infusion on Day 1 of 3 treatment cycles/additional 2 cycles (when applicable). Each cycle was 8 weeks apart (+2 weeks or up to +4 weeks in case of AE which had not adequately recovered).

Serious adverse events	Part A: 177Lu-IPN01072 4.5 GBq	Part B Cohort 1: 177Lu-IPN01072 6 GBq	Part B Cohort 3: 177Lu-IPN01072 4.5 GBq
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	1 / 6 (16.67%)	2 / 9 (22.22%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Precursor B-lymphoblastic lymphoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Tumour marker increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Presyncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B Cohort 6: 177Lu-IPN01072 4.5 GBq	All Participants	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	8 / 40 (20.00%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	1 / 1	1 / 1	
Malignant melanoma			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Precursor B-lymphoblastic lymphoma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Tumour marker increased			

subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Part A: 177Lu-IPN01072 4.5 GBq	Part B Cohort 1: 177Lu-IPN01072 6 GBq	Part B Cohort 3: 177Lu-IPN01072 4.5 GBq
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	6 / 6 (100.00%)	9 / 9 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	9 / 15 (60.00%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	13	0	5
Hot flush			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	5
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 15 (20.00%)	3 / 6 (50.00%)	2 / 9 (22.22%)
occurrences (all)	3	3	5
Fatigue			
subjects affected / exposed	9 / 15 (60.00%)	0 / 6 (0.00%)	3 / 9 (33.33%)
occurrences (all)	13	0	6
Feeling hot			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Infusion site reaction			
subjects affected / exposed	0 / 15 (0.00%)	2 / 6 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Malaise			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	1

Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	5
Chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injection site bruising			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injection site swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Sense of oppression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Xerosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	3
Epistaxis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lung cyst			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1

Affective disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Product issues			
Product leakage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 6 (0.00%)	4 / 9 (44.44%)
occurrences (all)	8	0	14
Platelet count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	4 / 9 (44.44%)
occurrences (all)	2	0	11
White blood cell count decreased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	5	0	6
C-reactive protein increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	2
Blood urea increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Protein urine present			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	4
White blood cell count increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Albumin urine present			

subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Blood potassium decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood potassium increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Blood pressure decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cortisol decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram ambulatory abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2

Liver function test increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Bilirubin urine present			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 15 (13.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
Fall			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Burn oesophageal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Occupational exposure to radiation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Palpitations			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Supraventricular extrasystoles			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Arrhythmia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ventricular extrasystoles			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 15 (33.33%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	7	0	3
Dizziness			
subjects affected / exposed	4 / 15 (26.67%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	5	1	1
Dysgeusia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	4	0	2
Lethargy			
subjects affected / exposed	3 / 15 (20.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	8	0	0
Paraesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Parosmia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Hypogeusia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Sensory disturbance			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 15 (20.00%)	3 / 6 (50.00%)	1 / 9 (11.11%)
occurrences (all)	10	13	4
Neutropenia			
subjects affected / exposed	2 / 15 (13.33%)	2 / 6 (33.33%)	1 / 9 (11.11%)
occurrences (all)	3	6	1
Anaemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Lymphopenia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 6 (33.33%)	2 / 9 (22.22%)
occurrences (all)	1	10	2
Leukopenia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	2	4	1
Lymph node pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Myelosuppression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Deafness unilateral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vestibular disorder			

subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	12 / 15 (80.00%)	1 / 6 (16.67%)	5 / 9 (55.56%)
occurrences (all)	24	1	13
Diarrhoea			
subjects affected / exposed	8 / 15 (53.33%)	1 / 6 (16.67%)	6 / 9 (66.67%)
occurrences (all)	18	1	14
Vomiting			
subjects affected / exposed	5 / 15 (33.33%)	0 / 6 (0.00%)	4 / 9 (44.44%)
occurrences (all)	8	0	12
Abdominal pain			
subjects affected / exposed	5 / 15 (33.33%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	7	1	2
Abdominal pain upper			
subjects affected / exposed	5 / 15 (33.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	5	1	0
Constipation			
subjects affected / exposed	4 / 15 (26.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	4	0	1
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Abdominal discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1

Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Stomatitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Abnormal faeces			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Anorectal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Breath odour			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Epigastric discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal motility disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Gingival bleeding			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Lip dry			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Steatorrhoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Hepatic pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	9 / 15 (60.00%)	2 / 6 (33.33%)	3 / 9 (33.33%)
occurrences (all)	14	2	3
Dry skin			
subjects affected / exposed	2 / 15 (13.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
Rash			
subjects affected / exposed	1 / 15 (6.67%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	1	1	2
Hyperhidrosis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Pruritus			

subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Rash papular			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Microalbuminuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 15 (20.00%)	1 / 6 (16.67%)	2 / 9 (22.22%)
occurrences (all)	5	1	5
Back pain			
subjects affected / exposed	5 / 15 (33.33%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	6	0	3
Musculoskeletal chest pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Arthritis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Groin pain			

subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Bone pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Coccydynia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Intervertebral disc protrusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 15 (20.00%)	1 / 6 (16.67%)	2 / 9 (22.22%)
occurrences (all)	3	1	2
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Anal fungal infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Groin abscess			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Perineal infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	2 / 15 (13.33%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part B Cohort 6: 177Lu-IPN01072 4.5 GBq	All Participants	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	39 / 40 (97.50%)	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 10 (10.00%)	12 / 40 (30.00%)	
occurrences (all)	3	21	
Hot flush			
subjects affected / exposed	3 / 10 (30.00%)	4 / 40 (10.00%)	
occurrences (all)	3	4	
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	7	
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 10 (50.00%)	13 / 40 (32.50%)	
occurrences (all)	11	22	
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	13 / 40 (32.50%)	
occurrences (all)	1	20	
Feeling hot			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Infusion site reaction			

subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Malaise			
subjects affected / exposed	2 / 10 (20.00%)	2 / 40 (5.00%)	
occurrences (all)	3	3	
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Chest discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	5	
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Discomfort			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Injection site bruising			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Injection site reaction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Injection site swelling			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Oedema peripheral			

subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Sense of oppression			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Xerosis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	2	2	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	1	5	
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Wheezing			
subjects affected / exposed	1 / 10 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Dyspnoea exertional			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Hiccups			

subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Lung cyst			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Affective disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Depressed mood			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Product issues			
Product leakage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 10 (0.00%)	7 / 40 (17.50%)	
occurrences (all)	0	22	
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	5 / 40 (12.50%)	
occurrences (all)	0	13	
White blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	4 / 40 (10.00%)	
occurrences (all)	0	11	
C-reactive protein increased			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	2	5	
Blood urea increased			

subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	3	
Protein urine present			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	5	
White blood cell count increased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Albumin urine present			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Blood potassium decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Blood potassium increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	3	
Blood pressure decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Cardiac murmur			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Cortisol decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Electrocardiogram ambulatory abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Liver function test increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Bilirubin urine present			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 10 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	4	
Fall			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Burn oesophageal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Occupational exposure to radiation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Cardiac disorders			

Tachycardia			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	2	5	
Palpitations			
subjects affected / exposed	1 / 10 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Arrhythmia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	1 / 10 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 10 (10.00%)	7 / 40 (17.50%)	
occurrences (all)	1	11	
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	6 / 40 (15.00%)	
occurrences (all)	0	7	
Dysgeusia			
subjects affected / exposed	1 / 10 (10.00%)	5 / 40 (12.50%)	
occurrences (all)	3	9	
Lethargy			
subjects affected / exposed	0 / 10 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	8	
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Parosmia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Syncope			

subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Taste disorder			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	4	
Hypogeusia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Sensory disturbance			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 10 (10.00%)	8 / 40 (20.00%)	
occurrences (all)	1	28	
Neutropenia			
subjects affected / exposed	1 / 10 (10.00%)	6 / 40 (15.00%)	
occurrences (all)	3	13	
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	5 / 40 (12.50%)	
occurrences (all)	2	6	
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)	5 / 40 (12.50%)	
occurrences (all)	0	13	
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	4 / 40 (10.00%)	
occurrences (all)	0	7	
Lymph node pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Myelosuppression			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Deafness neurosensory			

subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Deafness unilateral			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
External ear pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Vestibular disorder			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 10 (80.00%)	26 / 40 (65.00%)	
occurrences (all)	15	53	
Diarrhoea			
subjects affected / exposed	6 / 10 (60.00%)	21 / 40 (52.50%)	
occurrences (all)	8	41	
Vomiting			
subjects affected / exposed	6 / 10 (60.00%)	15 / 40 (37.50%)	
occurrences (all)	9	29	
Abdominal pain			
subjects affected / exposed	3 / 10 (30.00%)	10 / 40 (25.00%)	
occurrences (all)	4	14	
Abdominal pain upper			
subjects affected / exposed	2 / 10 (20.00%)	8 / 40 (20.00%)	
occurrences (all)	5	11	
Constipation			
subjects affected / exposed	1 / 10 (10.00%)	6 / 40 (15.00%)	
occurrences (all)	1	6	
Dyspepsia			
subjects affected / exposed	2 / 10 (20.00%)	4 / 40 (10.00%)	
occurrences (all)	2	4	

Flatulence			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 10 (20.00%)	3 / 40 (7.50%)	
occurrences (all)	3	4	
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Abdominal pain lower			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Abnormal faeces			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Anorectal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Breath odour			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Dental caries			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	

Epigastric discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Frequent bowel movements			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Gingival bleeding			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Lip dry			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Odynophagia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Paraesthesia oral			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Steatorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Toothache			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	3	
Hepatic pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	5 / 10 (50.00%)	19 / 40 (47.50%)	
occurrences (all)	5	24	
Dry skin			
subjects affected / exposed	1 / 10 (10.00%)	4 / 40 (10.00%)	
occurrences (all)	1	5	
Rash			
subjects affected / exposed	1 / 10 (10.00%)	4 / 40 (10.00%)	
occurrences (all)	1	5	
Hyperhidrosis			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Onychoclasis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Rash papular			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Microalbuminuria			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	7 / 40 (17.50%)	
occurrences (all)	2	13	
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	7 / 40 (17.50%)	
occurrences (all)	0	9	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 10 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Arthritis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Groin pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	4	
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Bone pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	3	
Coccydynia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	4	4	

Spinal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	7 / 40 (17.50%)	
occurrences (all)	1	7	
Bronchitis			
subjects affected / exposed	2 / 10 (20.00%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	2 / 10 (20.00%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Anal fungal infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Groin abscess			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Perineal infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Pharyngitis			

subjects affected / exposed	1 / 10 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Tooth abscess			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 10 (30.00%)	5 / 40 (12.50%)	
occurrences (all)	3	6	
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Increased appetite			
subjects affected / exposed	0 / 10 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2015	The protocol was amended to address feedback from different authorities and ethics committees. The protocol was also adapted according to standard procedures of the new owner, IPSEN Pharma. Changes included clarifications to inclusion and exclusion, adaptation of the activity escalation scheme to allow greater freedom to the Safety Review Board, removal of an exploratory evaluation of the somatostatin receptor scan, addition of computed tomography/magnetic resonance imaging at Week 12 after the first peptide receptor radionuclide therapy cycle, shifting the EOCT Visit from Week 28 to Week 24 and a number of administrative changes.
02 December 2015	The protocol was amended since the initially selected CRO Syneed Medidata was replaced as it entered an insolvency procedure and the sponsor did not want to take the risk of its bankruptcy during the conduct of the trial. The responsibility for pharmacovigilance and safety reporting was assumed by the sponsor leading to changes which were administrative in nature.
11 December 2015	The protocol was amended to specify that specific tumour and pituitary markers will be analysed in a central laboratory since some clinical sites do not have all these assessments in the repertoire of the local laboratory.
29 April 2016	The protocol was amended to consistently state that in the event of pregnancy the participant 'will' be withdrawn from treatment.
04 October 2016	The study population was updated. Exploratory objectives added. Several additional safety measures were included. Changes updated to figure 8, 9, 10 and 11. Changes updated to Table 5. Change in sponsor name, study administration section, sponsor approval signatory page and minor typographical changes for consistency throughout the protocol.
03 November 2017	Sponsor name updated, project coordinator and sponsor representative name corrected. Editorial changes applied. Extended screening period from 3 to 4 weeks. Confirmed the targeted radioactivity, confirmed that serum pregnancy test was to be done at Screening visit only. Clarification about pituitary markers. Entry criteria clarified. All changes listed above did not interfere with primary endpoint of the study and were done for clarification and to facilitate the recruitment and logistics for the participants and centers.

27 February 2018	Editorial changes made in order to put the protocol into the Ipsen template. Peptide mass dose escalation was added to Part B of the study with a design in two cohorts to evaluate if somatostatin receptor subtype 2 receptor saturation is occurring. The design in these two cohorts is a test-retest of increasing peptide at the second cycle to evaluate if receptor saturation is occurring. To carry out additional dose escalation of both peptide mass and radioactivity, eight cohorts have been developed with a step wise increase of peptide mass and radioactivity. The total number of participants in Part B increased. For Part B: Inclusion criteria modified and an exclusion criterion added; Additional changes applied to all participants from the time of implementation. Assessment of urine PK of IPN01072; Evaluation of systemic immune response and circulating markers added; Additional computed tomography (CT)/ magnetic resonance imaging and single-photon emission CT/CT scans added; Dosimetry assessments performed in additional cycles; Rules for delayed administration and treatment withdrawal changed; The list of conditions which were resolved was expanded. Change in tumor volume assessment added. Assessment of deoxyribonucleic acid double strand breaks in lymphocytes and tumour growth rate were removed. Tumour markers and PK parameters assessed were specified. The infusion rates and duration were revised. The volume of blood taken overall were updated. The urine collection time for dosimetric measurements were updated. Schedule of biopsy material collection specified. Details on action taken in case of spillage of investigational radiopharmaceutical product added. Participant withdrawal criteria specified. AE criteria specified. The introduction and study objectives updated.
24 July 2018	The protocol was amended to update the screening criteria (refining the inclusion and exclusion criteria) and contact details for the pharmacovigilance and coordinating investigator, to add precautions for handling radioactive material, to add a new assessment day (around Day 42) at which haematology and biochemistry were to be assessed and to make clarifications and corrections for consistency. Changes to clarify the interruption of somatostatin analogue therapy and criteria and safety monitoring that must be met for administering additional cycle were requested by the Food and Drug Administration.
07 May 2019	The protocol was amended to update personnel (sponsor’s representative and signatory), the infusion time/rate and other infusion-related procedures, to amend various assessments timings and clarify inclusion in the additional optional cycles, to amend dose escalation rules in case of toxicity, to specify urine sample collections in US and Canada sites, to amend AE/SAE reporting requirements, including in cases of laboratory abnormalities, to add definition and procedures for adverse event of special interest, to correct minor errors and make other clarifications.
13 August 2019	The protocol was amended to update the planned study period, to add an exploratory objective and endpoints to determine therapeutic efficacy using the modified RECIST , to clarify secondary endpoint related to tumour response, to clarify aspects related to the additional cycles (4 and 5) and amend their image reading to be done by a central laboratory, to define DLT definition in Part B, to clarify reporting procedures in “special situation” events, to clarify the decision process for administration of the additional cycles, to add AE reporting for IPN60070, to amend timing of assessments in Part B, to add screened participants population, to add interim analyses such that a total of three were to be performed and aid with cohort initiation decision, to correct minor errors and make other clarifications.

10 August 2020	The protocol was amended to clarify the 2-year long-term follow-up period. To add details of the option for participants to take part in a safety surveillance study after the long-term follow-up period is completed. To add an analysis of the 177Lu-IPN01072 dosimetry results according to the formula of the amino-acid solution administrated. To align the tumour response secondary endpoints (ORR, BOR, and DCR) with the statistical analysis plan. To change the secondary objective and secondary endpoint of changes in tumour volume to an exploratory objective and exploratory endpoint. To add DoR as an exploratory endpoint to further characterize the tumour response. To clarify the study populations (Safety Analysis set and ITT set) for analysis. To clarify the timing of the interim analyses and the clinical study report preparation. To clarify about coronavirus disease 2019 following the recent pandemic. To remove reference to the master protocol on the title page as, due to a change in the development strategy, the master protocol Ipsen 001 Version 1.0 has been closed. To align the synopsis and main body of the protocol for consistency. To correct minor errors and make other clarifications.

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.

Due to strategic reasons, the Ipsen management team decided to early terminate the D-FR-01072-001 / OPS-C-001 study. This decision was not due to any safety or tolerability concern, or any event associated with the use of the study drug.

Notes: