Clinical trial results:
An International Multicentre, Open-Label First in Human Phase I/II study to evaluate the safety, tolerability, biodistribution and antitumour activity of 177Lu-3BP-227 for the treatment of subjects with solid tumours expressing neurotensin receptor 1

Summary

EudraCT number	2017-001263-20
Trial protocol	BE NL
Global end of trial date	28 April 2021

Results information

Result version number	v1 (current)
This version publication date	08 May 2022
First version publication date	08 May 2022

Trial information

Trial identification

Sponsor protocol code	D-FR-01087-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03525392
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma SAS
Sponsor organisation address	65, quai Georges Gorse, Boulogne-Billancourt, France, 92100
Public contact	Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma SAS, 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	28 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase 1: To establish the safety and tolerability of fractionated intravenous (IV) administrations of 177Lu-3BP-227 in participants with unresectable, locally advanced or metastatic cancers expressing neurotensin receptor 1 (NTSR1).

Phase 2: To estimate objective response rate (ORR) of fractionated IV administrations of 177Lu-3BP-227 in participants with unresectable, locally advanced or metastatic cancers expressing NTSR1.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki and in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use 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	03 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	14
EEA total number of subjects	10

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 1/2 first in human study was conducted in participants with unresectable, locally advanced or metastatic solid tumors expressing NTSR1 at 9 investigational sites. The sponsor terminated the study early during Cohort 5 in phase 1 dose escalation; phase 1 dose expansion and phase 2 were not started.

Pre-assignment

Screening details:

For phase 1, core trial was up to 19 weeks and comprised of 2 treatment cycles. If a participant had clinical benefit, they could receive up to 4 additional cycles after end of core trial (EOCT). Due to early termination, only results of core trial are presented. 14 participants received a therapeutic dose of 177Lu-3BP-227 in phase 1 of the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: 177Lu-3BP-227 2.5 GBq

Arm description:

Participants received 177Lu-3BP-227 2.5 Gigabecquerel (GBq) fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

Arm type	Experimental
Investigational medicinal product name	177Lu-3BP-227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 2.5 GBq of 177Lu-3BP-227 in a total volume of 20 milliliter (mL) that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

Arm title	Cohort 2: 177Lu-3BP-227 4.0 GBq

Arm description:

Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

Arm type	Experimental
Investigational medicinal product name	177Lu-3BP-227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 4.0 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

Arm title	Cohort 3: 177Lu-3BP-227 5.5 GBq

Arm description:

Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5

weeks during the core trial period.

Arm type	Experimental
Investigational medicinal product name	177Lu-3BP-227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 5.5 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

Arm title	Cohort 4: 177Lu-3BP-227 6.5 GBq

Arm description:

Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

Arm type	Experimental
Investigational medicinal product name	177Lu-3BP-227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 6.5 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

Arm title	Cohort 5: 177Lu-3BP-227 7.5 GBq

Arm description:

Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

Arm type	Experimental
Investigational medicinal product name	177Lu-3BP-227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The study medication formulation consisted of 7.5 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

Number of subjects in period 1	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq
Started	2	3	5
Completed	1	2	2
Not completed	1	1	3
Adverse event, non-fatal	1	-	2
Progressive disease	-	1	1

Number of subjects in period 1	Cohort 4: 177Lu-3BP-227 6.5 GBq	Cohort 5: 177Lu-3BP-227 7.5 GBq

Started	3	1
Completed	0	0
Not completed	3	1
Adverse event, non-fatal	-	-
Progressive disease	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: 177Lu-3BP-227 2.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 2.5 Gigabecquerel (GBq) fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 2: 177Lu-3BP-227 4.0 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 3: 177Lu-3BP-227 5.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 4: 177Lu-3BP-227 6.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 5: 177Lu-3BP-227 7.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	

Reporting group values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq
Number of subjects	2	3	5
Age categorical Units: Subjects			
Age continuous			
99999 = Standard deviation cannot be calculated when only 1 participant analyzed.			
Units: years			
arithmetic mean	70.0	64.3	64.0
standard deviation	± 4.2	± 16.2	± 7.2
Gender categorical Units: Subjects			
Female	0	1	1
Male	2	2	4
Race Units: Subjects			
Not Collected	2	3	5
White	0	0	0
Asian	0	0	0
Black / African American	0	0	0
Native Hawaiian / Other Pacific Islander	0	0	0
American Indian / Alaska Native	0	0	0
Other	0	0	0
Ethnicity Units: Subjects			

Hispanic or Latino	0	0	0
Not Hispanic or Latino	2	3	5

Reporting group values	Cohort 4: 177Lu-3BP-227 6.5 GBq	Cohort 5: 177Lu-3BP-227 7.5 GBq	Total
Number of subjects	3	1	14
Age categorical Units: Subjects			
Age continuous			
99999 = Standard deviation cannot be calculated when only 1 participant analyzed.			
Units: years			
arithmetic mean	66.3	77.0	
standard deviation	± 9.1	± 99999	-
Gender categorical Units: Subjects			
Female	2	0	4
Male	1	1	10
Race Units: Subjects			
Not Collected	0	0	10
White	3	1	4
Asian	0	0	0
Black / African American	0	0	0
Native Hawaiian / Other Pacific Islander	0	0	0
American Indian / Alaska Native	0	0	0
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	1	14

End points

End points reporting groups

Reporting group title	Cohort 1: 177Lu-3BP-227 2.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 2.5 Gigabecquerel (GBq) fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 2: 177Lu-3BP-227 4.0 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 3: 177Lu-3BP-227 5.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 4: 177Lu-3BP-227 6.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 5: 177Lu-3BP-227 7.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Subject analysis set title	All Participants
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received 177Lu-3BP-227 dose range of 2.5 to 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	

Primary: Phase 1: Number of Participants With Dose-Limiting Toxicities (DLT)

End point title	Phase 1: Number of Participants With Dose-Limiting Toxicities (DLT)[1]
End point description:	
DLTs were defined for a list of predefined study medication-related adverse events (AEs) as specified in the protocol, according to the National Cancer Institute – Common Terminology Criteria for Adverse Events scale version 5.0 (CTCAE v5.0) that occurred during the defined DLT assessment period (during Cycle 1 or 2). Safety population contained all participants who received at least 1 dose of study medication.	
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:

[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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	5	3
Units: participants	0	0	0	0

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximum Uptake (%) of 177Lu-3BP-227 at Target Lesions and Discernible Organs

End point title	Phase 1: Maximum Uptake (%) of 177Lu-3BP-227 at Target Lesions and Discernible Organs

End point description:

177Lu-3BP-227 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, left kidney, right kidney, healthy liver, and spleen) was determined. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Here, n = number of observations for both cycles.

End point type	Secondary

End point timeframe:

Measurements were performed at 0 to 1 hours, 2 to 4 hours, 16 to 24 hours, 40 to 48 hours, 72 to 96 hours post infusion in each treatment cycle.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percentage of 177Lu-3BP-227				
median (full range (min-max))				
All cycles: Body (n= 21)	99.7 (99.2 to 100)			
All cycles: Bone marrow (n= 20)	1.10 (0.560 to 1.98)			
All cycles: Left kidney (n= 25)	0.247 (0.130 to 0.409)			
All cycles: Right kidney (n= 25)	0.227 (0.129 to 0.452)			
All cycles: Healthy liver (n= 20)	1.01 (0.0760 to 1.84)			
All cycles: Spleen (n= 17)	0.280 (0.110 to 0.770)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximal Concentration (Cmax) of 177Lu-3BP-227

End point title	Phase 1: Maximal Concentration (Cmax) of 177Lu-3BP-227

End point description:

The pharmacokinetic (PK) sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood and organs/lesions were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[2]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[2] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time Post Injection to Achieve Cmax of 177Lu-3BP-227

End point title	Phase 1: Time Post Injection to Achieve Cmax of 177Lu-3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood, urine and organs/lesions were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[3]			
Units: not applicable				
median (full range (min-max))	(to)			

Notes:

[3] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Plasma Concentration Versus Time Curve (AUC) of 177Lu-3BP-227

End point title	Phase 1: Area Under the Plasma Concentration Versus Time Curve (AUC) of 177Lu-3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood, urine and organs/lesions were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[4]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[4] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Half-life (t1/2) of 177Lu-3BP-227

End point title	Phase 1: Half-life (t1/2) of 177Lu-3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood, urine and organs/lesions were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[5]			
Units: not applicable				
median (full range (min-max))	(to)			

Notes:

[5] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Number of Participants With Highest Absorbed Dose of 177Lu-3BP-227 to Each Discernible Organ

End point title	Phase 1: Number of Participants With Highest Absorbed Dose of 177Lu- 3BP-227 to Each Discernible Organ

End point description:

The absorbed dose to the target lesions and discernible organs (i.e., organs showing uptake) was evaluated by image-based analysis. The organs considered for 177Lu-3BP-227 image-based dosimetry assessment included: healthy liver, total liver, bone marrow, left kidney, right kidney, intestine (large and small), spleen, pancreas, stomach wall, right ovary, left ovary, uterus, right testis, left testis, thymus, right thyroid gland, left thyroid gland, prostate gland and total body. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Here, n= number of participants analyzed for each specific organ/cycle.

End point type	Secondary

End point timeframe:

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

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: participants				
Cycle 1: Right kidney (n= 14)	4			
Cycle 1: Left kidney (n= 14)	3			
Cycle 1: Large intestine (n= 14)	5			
Cycle 1: Bladder (n= 14)	2			
Cycle 1: Lymph node (n= 14)	0			
Cycle 2: Right kidney (n= 11)	2			
Cycle 2: Left kidney (n= 11)	2			
Cycle 2: Large intestine (n= 11)	4			
Cycle 2: Bladder (n= 11)	2			
Cycle 2: Lymph node (n= 11)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Specific Absorbed Dose to the Target Lesions of 177Lu-3BP-227

End point title	Phase 1: Specific Absorbed Dose to the Target Lesions of 177Lu-3BP-227

End point description:

The specific absorbed dose to the target lesions was evaluated by image-based analysis. Results for all studied diseases (pancreatic ductal adenocarcinoma and colorectal carcinoma) at all anatomical locations (cervical, intrapelvic, liver, lung, lymphenode, and pancreas) for all cycles (Cycle 1 and 2) are reported. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis.

End point type	Secondary

End point timeframe:

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

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	14[6]			
Units: Gray/GBq				
median (full range (min-max))	0.183 (0.0551 to 1.21)			

Notes:

[6] - 47 Lesions.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Specific Absorbed Dose Per Organ of 177Lu-3BP-227

End point title	Phase 1: Specific Absorbed Dose Per Organ of 177Lu-3BP-227

End point description:

The specific absorbed dose per organ was evaluated by image-based analysis. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Here, n = number of observations for both cycles.

End point type	Secondary

End point timeframe:

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

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Gray/GBq				
median (full range (min-max))				
All cycles: Bone marrow (n= 25)	0.0636 (0.0346 to 0.0943)			
All cycles: Healthy liver (n= 25)	0.0515 (0.0263 to 0.0811)			

All cycles: Left kidney (n= 25)	0.255 (0.102 to 1.05)			
All cycles: Right kidney (n= 25)	0.242 (0.118 to 0.943)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Cumulative Absorbed Organ Doses of 177Lu-3BP-227

End point title	Phase 1: Cumulative Absorbed Organ Doses of 177Lu-3BP-227

End point description:

The cumulative absorbed dose to the discernible organs (i.e., organs showing uptake) was evaluated by image-based analysis. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Cumulative absorbed doses on Cycles 1 and 2 are only presented for participants who have performed the 2 cycles.

End point type	Secondary

End point timeframe:

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

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	3	3
Units: Gray				
median (full range (min-max))				
Cycle 2: Bone marrow	0.326 (0.326 to 0.326)	0.604 (0.304 to 0.645)	0.680 (0.391 to 0.837)	0.820 (0.628 to 1.11)
Cycle 2: Healthy liver	0.254 (0.254 to 0.254)	0.353 (0.271 to 0.415)	0.530 (0.428 to 0.637)	0.714 (0.469 to 0.927)
Cycle 2: Left kidney	2.17 (2.17 to 2.17)	4.19 (1.38 to 6.21)	3.33 (1.90 to 5.12)	3.44 (1.90 to 3.48)
Cycle 2: Right kidney	2.38 (2.38 to 2.38)	3.39 (1.53 to 5.51)	2.97 (2.14 to 5.74)	3.01 (2.00 to 4.67)

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Gray				
median (full range (min-max))				
Cycle 2: Bone marrow	0.694 (0.694 to 0.694)			
Cycle 2: Healthy liver	0.571 (0.571 to 0.571)			
Cycle 2: Left kidney	2.95 (2.95 to 2.95)			

Cycle 2: Right kidney	2.92 (2.92 to 2.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Cmax of 3BP-227

End point title	Phase 1: Cmax of 3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[7]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[7] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: AUC of 3BP-227

End point title	Phase 1: AUC of 3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[8]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[8] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: t1/2 of 3BP-227

End point title	Phase 1: t1/2 of 3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[9]			
Units: not applicable				
median (full range (min-max))	(to)			

Notes:

[9] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Clearance of 3BP-227

End point title	Phase 1: Clearance of 3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[10]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[10] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Volume of Distribution of 3BP-227

End point title	Phase 1: Volume of Distribution of 3BP-227

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[11]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[11] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Cumulative Amount of Unchanged 3BP-227 Excreted Into the Urine

End point title	Phase 1: Cumulative Amount of Unchanged 3BP-227 Excreted Into the Urine

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

End point type	Secondary

End point timeframe:

For other sites, from the start of the infusion to 6 hours, 6 to 12 hours, 12 to 24 hours, and 24 to 48 hours post infusion of 177Lu-3BP-227 in Cycle 1; For USA sites, from the start of the infusion to 6 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[12]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[12] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Renal Clearance of 3BP-227 From Plasma

End point title	Phase 1: Renal Clearance of 3BP-227 From Plasma

End point description:

The CLR of 3BP-227 was evaluated. The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 for each treatment cycle. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated.

End point type	Secondary

End point timeframe:

For other sites, from the start of the infusion to 6 hours, 6 to 12 hours, 12 to 24 hours, and 24 to 48 hours post infusion of 177Lu-3BP-227 in Cycle 1; For USA sites, from the start of the infusion to 6 hours post infusion of 177Lu-3BP-227 in Cycle 1.

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[13]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[13] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Number of Participants With ORR

End point title	Phase 1: Number of Participants With ORR

End point description:

The ORR was defined as number of participants with a best overall response (BOR) characterized as either a complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) relative to the total number of evaluable participants. Primary Pharmacodynamic population (for tumor response) included all participants who received at least 2 therapeutic doses of 177Lu-3BP-227 and reached the end of Cycle 2 or EOCT visit with available postbaseline tumor assessment based on RECIST 1.1 and with no major protocol deviations with an impact on the analysis.

End point type	Secondary

End point timeframe:

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

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	2	1
Units: participants	0	1	0	0

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Number of Participants With Disease Control Rate (DCR)

End point title	Phase 1: Number of Participants With Disease Control Rate (DCR)

End point description:

The DCR was defined as number of participants with a BOR characterized as CR, PR or stable disease according to RECIST 1.1 relative to the total number of evaluable participants. Primary Pharmacodynamic population (for tumor response) included all participants who received at least 2 therapeutic doses of 177Lu-3BP-227 and reached the end of Cycle 2 or EOCT visit with available postbaseline tumor assessment based on RECIST 1.1 and with no major protocol deviations with an impact on the analysis.

End point type	Secondary

End point timeframe:

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

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	2	1
Units: participants	0	1	0	0

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Progression-Free Survival (PFS)

End point title	Phase 1: Progression-Free Survival (PFS)

End point description:

The PFS was defined as the time from date of first study medication administration until progression, according to RECIST 1.1. Due to the early termination of the study, survival analysis on PFS was not performed.

End point type	Secondary

End point timeframe:

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

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[14]	0[15]	0[16]	0[17]
Units: participants				

Notes:

[14] - Early termination of the study.

[15] - Early termination of the study.

[16] - Early termination of the study.

[17] - Early termination of the study.

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	0[18]			
Units: participants				

Notes:

[18] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Overall Survival (OS)

End point title	Phase 1: Overall Survival (OS)

End point description:

The OS was defined from first study medication administration until death, according to RECIST 1.1. Due to the early termination of the study, survival analysis on OS was not performed.

End point type	Secondary

End point timeframe:

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

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[19]	0[20]	0[21]	0[22]
Units: participants				

Notes:

[19] - Early termination of the study.

[20] - Early termination of the study.

[21] - Early termination of the study.

[22] - Early termination of the study.

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	0[23]			
Units: participants				

Notes:

[23] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Metabolic Tumor Response Using Positron Emission Tomography (PET) Response Criteria In Solid Tumors (PERCIST) Version 1.0 or Practical PERCIST

End point title	Phase 1: Metabolic Tumor Response Using Positron Emission Tomography (PET) Response Criteria In Solid Tumors (PERCIST) Version 1.0 or Practical PERCIST

End point description:

Tumor response assessments were planned to perform by the site investigator (local) for the phase 1 and dose escalation part and by independent reader (central) for the phase 2. All fluorine-18 fluorodeoxyglucose-PET images were used for the metabolic tumor response assessments as described in PERCIST version 1.0 by the Investigator and/or independent readers. Due to the early termination of the study, metabolic tumor response was not performed.

End point type	Secondary

End point timeframe:

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

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	0[24]			
Units: not applicable				
arithmetic mean (standard deviation)	()			

Notes:

[24] - Early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Tumor Marker Levels in Serum - Cancer Antigen 19-9

End point title	Phase 1: Tumor Marker Levels in Serum - Cancer Antigen 19-9

End point description:

Changes in tumor markers in serum relevant and specific to the underlying tumor disease was determined. Pharmacodynamic population included all participants who received at least 1 therapeutic dose and with available post-baseline pharmacodynamics/efficacy data. Here, n = number of participants analyzed at each specific time point, 99999 = no participants analyzed and 9999 = standard deviation cannot be calculated when only 1 participant analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, EOCT (maximum of 16 weeks) and early withdrawal.

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	5	3
Units: international units/milliliter				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)	50019.00 (± 70683.81)	13.00 (± 9999)	20939.54 (± 46482.66)	1455.50 (± 78.49)
Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)	66.00 (± 9999)	456.33 (± 753.23)	277.90 (± 239.71)	18420.33 (± 27442.99)
EOCT (n= 1, 2, 1, 1, 1)	112.00 (± 9999)	928.00 (± 1294.01)	1166.90 (± 9999)	3532.00 (± 9999)
Early withdrawal (n= 0, 0, 2, 1, 0)	99999 (± 99999)	99999 (± 99999)	64.90 (± 86.41)	8398.00 (± 9999)

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	1			

Units: international units/milliliter				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)	314.70 (± 9999)			
Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)	490.50 (± 9999)			
EOCT (n= 1, 2, 1, 1, 1)	629.90 (± 9999)			
Early withdrawal (n= 0, 0, 2, 1, 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Tumor Marker Levels in Serum - Carcinoembryonic Antigen

End point title	Phase 1: Tumor Marker Levels in Serum - Carcinoembryonic Antigen

End point description:

Changes in tumor markers in serum relevant and specific to the underlying tumor disease was determined. Pharmacodynamic population included all participants who received at least 1 therapeutic dose and with available post-baseline pharmacodynamics/efficacy data. Here, n = number of participants analyzed at each specific time point, 99999 = no participants analyzed and 9999 = standard deviation cannot be calculated when only 1 participant analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, EOCT (maximum of 16 weeks) and early withdrawal.

End point values	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq	Cohort 4: 177Lu-3BP-227 6.5 GBq
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	5	3
Units: microgram per liter				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)	857.95 (± 1209.22)	117.40 (± 9999)	112.38 (± 94.41)	6.65 (± 7.14)
Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)	3.20 (± 9999)	37.93 (± 41.01)	210.97 (± 213.86)	47.87 (± 62.85)
EOCT (n= 1, 2, 1, 1, 1)	4.30 (± 9999)	75.50 (± 47.09)	321.20 (± 9999)	184.00 (± 9999)
Early withdrawal (n= 0, 0, 2, 1, 0)	99999 (± 99999)	99999 (± 99999)	53.75 (± 23.83)	29.60 (± 9999)

End point values	Cohort 5: 177Lu-3BP-227 7.5 GBq			
Subject group type	Reporting group			
Number of subjects analysed	1			

Units: microgram per liter				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)	3.50 (± 9999)			
Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)	4.60 (± 9999)			
EOCT (n= 1, 2, 1, 1, 1)	5.10 (± 9999)			
Early withdrawal (n= 0, 0, 2, 1, 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent AEs are reported for participants who received the therapeutic dose of 177Lu-32P-227 during the core trial (Cycle 1 Day 1 up to EOCT); maximum of 16 weeks.	
Adverse event reporting additional description:	
Safety population contained all participants who received at least 1 dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Cohort 1: 177Lu-3BP-227 2.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 2.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 2: 177Lu-3BP-227 4.0 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 3: 177Lu-3BP-227 5.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 4: 177Lu-3BP-227 6.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	
Reporting group title	Cohort 5: 177Lu-3BP-227 7.5 GBq
Reporting group description:	
Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.	

Serious adverse events	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 3 (66.67%)	5 / 5 (100.00%)
number of deaths (all causes)	1	0	2
number of deaths resulting from adverse events	1	0	2
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	3 / 5 (60.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
General physical health deterioration			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Enterocolitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Large intestinal obstruction			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Subileus			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (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
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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			
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Infections and infestations			
Hepatic infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (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

Serious adverse events	Cohort 4: 177Lu-3BP-227 6.5 GBq	Cohort 5: 177Lu-3BP-227 7.5 GBq	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Subileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Hepatic infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: 177Lu-3BP-227 2.5 GBq	Cohort 2: 177Lu-3BP-227 4.0 GBq	Cohort 3: 177Lu-3BP-227 5.5 GBq
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	3 / 3 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Venous thrombosis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	2
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
General physical health deterioration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Illusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	3
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood urea increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	3
C-reactive protein increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	0 / 5 (0.00%)
occurrences (all)	2	4	0
Haematocrit decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	1 / 5 (20.00%)
occurrences (all)	2	7	1
Neutrophil count decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Platelet count decreased			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Protein total increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Red blood cell count decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	4 / 5 (80.00%)
occurrences (all)	0	1	5
White blood cell count decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	4	0	1

Injury, poisoning and procedural complications			
Product prescribing error			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	3 / 5 (60.00%)
occurrences (all)	1	4	6
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	2 / 5 (40.00%)
occurrences (all)	1	1	3
Anal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Ileus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Small intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	2 / 5 (40.00%)
occurrences (all)	0	1	3
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Jaundice			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	2 / 5 (40.00%)
occurrences (all)	0	1	3
Musculoskeletal stiffness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Polyarthritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Hypercalcaemia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	4 / 5 (80.00%)
occurrences (all)	0	1	8
Hypernatraemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	1	2
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypocalcaemia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypokalaemia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	3

Non-serious adverse events	Cohort 4: 177Lu-3BP-227 6.5 GBq	Cohort 5: 177Lu-3BP-227 7.5 GBq	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	0 / 1 (0.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Venous thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Illusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood bicarbonate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood cholesterol increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Haematocrit decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Protein total increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Red blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Product prescribing error			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Anal haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Ileus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Small intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Polyarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2017	The protocol was amended to update tumor biopsy inclusion criteria as per review by the Ethical Committee in France.
09 November 2017	The protocol was amended to incorporate changes to inclusion criteria, dose escalation part, physical examination and electrocardiogram assessments as per review by the Health Authorities in France.
06 December 2017	The protocol was amended to include Ewing sarcoma as an additional indication in the phase 1/2 study and to provide updated information regarding the study medication.
02 March 2018	The protocol was amended to give precision on the calculation of the tumor growth rate, information about drug-drug interactions, clarification of discontinuation process, information about infusion rate in response to AEs and increase time for use of contraception for females in the inclusion criteria from 30 days to 6 months, as well as information about spillages.
17 July 2018	The protocol was amended to improve the determination of the biokinetics of 177Lu-3BP-227 and perform an absolute quantification of radioactivity in target organs. Whole body scans (planar scintigraphy) were added to single photon emission computed tomography during treatment period. Whole body scans would allow the calculation of whole-body time-integrated activity coefficient ("residence time") that was needed for dosimetry analysis, as it accounts for nonspecific activity in the body. Inclusion criterion was updated to enable the recruitment of participants who did not have a compelling standard-of-care option.
20 June 2019	The protocol was amended to update personnel (the sponsor-authorized protocol approver and sponsor medical monitor), to update the background information, especially new nonclinical toxicology data, to update the number of participants receiving screening and therapeutic dose, to remove tumor growth rate and add genomic alterations in circulating cell-free DNA and gene mutation status as exploratory objectives and endpoints, to change pharmacokinetic timepoints to improve the clinical feasibility, to specify the biopsy conditions and put them as optional assessments, to remove tumor markers assessments for gastric cancer (serum cancer antigen 72-4) and squamous-cell carcinoma of head and neck (tissue polypeptide antigen), to refine the exclusion criteria regarding body weight, to clarify discontinuation rules, to clarify the duration of the safety follow-up period after the study medication screening dose administration and the reporting of AE collection after the last study medication administration, to specify that death due to disease progression will be reported as an SAE, to specify details on the preparation of the clinical study report, and to add schedule of assessments for screen failure participants. In addition, the recording of safety laboratory test results was changed from recording "any AEs according to National Cancer Institute-CTCAE" to "abnormalities in laboratory test values should only be reported as AEs if any of the following apply: • They resulted in a change in study medication schedule of administration (change in dosage, delay in administration, study medication discontinuation). • They required intervention or a diagnosis evaluation to assess the risk to the participant. • They were considered as clinically significant by the Investigator, or the laboratory test abnormality suggested a disease and/or organ toxicity that was new or had worsened from baseline based on sponsor review.

12 June 2020	The protocol was amended to update the following: • Clarify the inclusion criteria for participant selection as follows: - To clearly state nonresectable locally advanced disease. - To clearly state that no further suitable treatment options were available for participants eligible for the study. • Allow participants screened and found positive for NTSR1 in the 111In-IPN01087 phase 1 diagnostic study to take part in this study without having the diagnostic dose of 177Lu-3BP-227 during the Screening phase. • Extend the long-term follow-up period from 2 years to a maximum of 5 years or until lost to follow-up, withdrawal of consent or death, whichever occurred first. • Revise the DLT criteria to adequately describe the grading as stated in the CTCAE v5.0 dictionary. • Revise the participant discontinuation rules so if there were life-threatening toxicities outside of the DLT period, treatment was discontinued. • Optimize the dosimetry evaluation through adaptation of the imaging schedule. • Clarify biopsy collection. • Clarify about COVID-19 added following the recent pandemic. • Remove the exploratory endpoint of DNA-double strand breaks in peripheral lymphocytes.

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.

The sponsor terminated the study early and phase 1 dose expansion and phase 2 were not started. The decision to terminate the study was not due to any safety or tolerability concern, or any event associated with the use of 177Lu-3BP-227.

Notes: