Clinical trial results:
A Phase I/II open-label, multi-center, dose-escalation study of safety, tolerability, pharmacokinetics, dosimetry, and response to repeat dosing of 177Lu-PSMA-R2 radio-ligand therapy in patients with prostate specific membrane antigen (PSMA) positive (68Ga-PSMA-R2) progressive metastatic castration-resistant prostate cancer, following previous systemic treatment.

Summary

EudraCT number	2017-004034-29
Trial protocol	GB ES
Global end of trial date	02 June 2022

Results information

Result version number	v1 (current)
This version publication date	09 March 2023
First version publication date	09 March 2023

Trial information

Trial identification

Sponsor protocol code	A206T-G01-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03490838
WHO universal trial number (UTN)	-
Other trial identifiers	CAAA602A12101: Novartis

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland, 4002
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	02 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 June 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This Phase I/II study was intended to investigate the safety, tolerability, and radiation dosimetry of 177Lu-PSMA-R2 and further assess preliminary efficacy data in patients with Metastatic Castration-resistant Prostate Cancer (mCRPC). The Phase I portion of the study aimed to determine the recommended dose or Maximum Tolerated Dose (MTD) of 177Lu-PSMA-R2 for Radio-Ligand Therapy (RLT) of mCRPC, and the Phase II portion was planned to expand into approximately 60 patients documenting the preliminary activity (anti-tumor response) of repeated treatments administered, continuing safety assessments and collecting Quality of Life (QoL) data.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	27
EEA total number of subjects	6

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)	8
From 65 to 84 years	18
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted at 11 centers in 2 countries: Spain (2) and USA (9).

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	Phase I: Dose Escalation Cohort 1

Arm description:

Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)

Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:

3 cycles at 100 mCi

Arm title	Phase I: Dose Escalation Cohort 2

Arm description:

Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)

Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:

3 cycles at 200 mCi

Arm title	Phase I: Dose Escalation Cohort 3A

Arm description:

Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)

Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:

4 cycles at 200 mCi

Arm title	Phase I: Dose Escalation Cohort 3B

Arm description:	
Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	
Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use
Dosage and administration details:	
3 cycles at 300 mCi	
Arm title	Phase I: Dose Escalation Cohort 4B
Arm description:	
Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	
Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use
Dosage and administration details:	
4 cycles at 300 mCi	
Arm title	Phase I: Dose Escalation Cohort 4C
Arm description:	
Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	
Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use
Dosage and administration details:	
3 cycles at 400 mCi	
Arm title	Phase I: Dose Escalation Cohort 5C
Arm description:	
Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	
Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use
Dosage and administration details:	
4 cycles at 400 mCi	
Arm title	Phase I: Dose Escalation Cohort 5D
Arm description:	
Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	
Arm type	Experimental

Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:

2 cycles at 500 mCi

Arm title	Phase I: Dose Escalation Cohort 6E

Arm description:

Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)

Arm type	Experimental
Investigational medicinal product name	177Lu-PSMA-R2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:

3 cycles at 500 mCi

Number of subjects in period 1	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A
Started	3	3	3
Completed	0	0	0
Not completed	3	3	3
Adverse event, serious fatal	1	1	1
Consent withdrawn by subject	2	2	1
Physician decision	-	-	-
Other pre-specified reason defined in the protocol	-	-	-
Sponsor Decision	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C
Started	3	3	3
Completed	0	0	0
Not completed	3	3	3
Adverse event, serious fatal	3	3	2
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Other pre-specified reason defined in the protocol	-	-	-
Sponsor Decision	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E

Started	3	3	3
Completed	0	0	0
Not completed	3	3	3
Adverse event, serious fatal	1	1	-
Consent withdrawn by subject	-	-	-
Physician decision	-	2	1
Other pre-specified reason defined in the protocol	-	-	1
Sponsor Decision	1	-	1
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Phase I: Dose Escalation Cohort 1
Reporting group description:	
Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 2
Reporting group description:	
Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 3A
Reporting group description:	
Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 3B
Reporting group description:	
Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 4B
Reporting group description:	
Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 4C
Reporting group description:	
Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 5C
Reporting group description:	
Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 5D
Reporting group description:	
Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 6E
Reporting group description:	
Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)	

Reporting group values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A
Number of subjects	3	3	3
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)	2	2	0
From 65-84 years	1	1	2
85 years and over	0	0	1
Age Continuous Units: Years			
arithmetic mean	58.3	61.0	74.0

standard deviation	± 12.01	± 5.57	± 10.44

Sex: Female, Male Units: Participants			
Female	0	0	0
Male	3	3	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	3	3
More than one race	1	0	0
Unknown or Not Reported	0	0	0
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.			
Units: Subjects			
Grade 0	3	3	1
Grade 1	0	0	2
Number of participants by Total Gleason score (>=6)			
Gleason score can range from 2-10. The higher the Gleason Score, the more likely that the cancer will grow and spread quickly. Scores of 6 (or less) describe cancer cells that look similar to normal cells and suggest that the cancer is likely to grow slowly. A score of 7 suggests an intermediate risk for aggressive cancer. Scores of 8 (or higher) describe cancers that are likely to spread more rapidly, these cancers are often referred to as poorly differentiated or high grade.			
Units: Subjects			
Gleason score = 6	0	0	0
Gleason score = 7	1	1	1
Gleason score = 8	1	0	0
Gleason score = 9	0	2	1
Gleason score = 10	0	0	0
Gleason score = Missing	1	0	1
Time since first prostate cancer diagnosis			
Time since first prostate cancer diagnosis is defined as (date of screening – date of first prostate cancer diagnosis + 1) / 30.4375.			
Units: Months			
arithmetic mean	70.5	76.7	176.6
standard deviation	± 52.95	± 26.44	± 132.16

Reporting group values	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C
Number of subjects	3	3	3
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)	0	0	1
From 65-84 years	3	3	2
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	72.7	72.0	65.7
standard deviation	± 6.03	± 2.00	± 2.31
Sex: Female, Male			
Units: Participants			
Female	0	0	0
Male	3	3	3
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	3	2	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.			
Units: Subjects			
Grade 0	0	2	3
Grade 1	3	1	0
Number of participants by Total Gleason score (>=6)			
Gleason score can range from 2-10. The higher the Gleason Score, the more likely that the cancer will grow and spread quickly. Scores of 6 (or less) describe cancer cells that look similar to normal cells and suggest that the cancer is likely to grow slowly. A score of 7 suggests an intermediate risk for aggressive cancer. Scores of 8 (or higher) describe cancers that are likely to spread more rapidly, these cancers are often referred to as poorly differentiated or high grade.			
Units: Subjects			
Gleason score = 6	0	1	0
Gleason score = 7	0	1	1
Gleason score = 8	1	0	1
Gleason score = 9	1	1	1
Gleason score = 10	1	0	0
Gleason score = Missing	0	0	0
Time since first prostate cancer diagnosis			
Time since first prostate cancer diagnosis is defined as (date of screening – date of first prostate cancer diagnosis + 1) / 30.4375.			
Units: Months			
arithmetic mean	75.3	89.4	40.0

standard deviation	± 54.27	± 49.80	± 15.47

Reporting group values	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Number of subjects	3	3	3
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)	1	1	1
From 65-84 years	2	2	2
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	67.0	64.7	64.3
standard deviation	± 6.08	± 5.86	± 8.14
Sex: Female, Male Units: Participants			
Female	0	0	0
Male	3	3	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.			
Units: Subjects			
Grade 0	1	2	3
Grade 1	2	1	0
Number of participants by Total Gleason score (>=6)			
Gleason score can range from 2-10. The higher the Gleason Score, the more likely that the cancer will grow and spread quickly. Scores of 6 (or less) describe cancer cells that look similar to normal cells and suggest that the cancer is likely to grow slowly. A score of 7 suggests an intermediate risk for aggressive cancer. Scores of 8 (or higher) describe cancers that are likely to spread more rapidly, these cancers are often referred to as poorly differentiated or high grade.			
Units: Subjects			

Gleason score = 6	0	0	0
Gleason score = 7	0	3	2
Gleason score = 8	1	0	1
Gleason score = 9	1	0	0
Gleason score = 10	1	0	0
Gleason score = Missing	0	0	0
Time since first prostate cancer diagnosis			
Time since first prostate cancer diagnosis is defined as (date of screening – date of first prostate cancer diagnosis + 1) / 30.4375.			
Units: Months			
arithmetic mean	129.5	76.1	120.2
standard deviation	± 78.29	± 32.37	± 49.29

Reporting group values	Total		
Number of subjects	27		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	8		
From 65-84 years	18		
85 years and over	1		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	0		
Male	27		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	25		
More than one race	1		
Unknown or Not Reported	0		
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.			
Units: Subjects			

Grade 0	18		
Grade 1	9		
Number of participants by Total Gleason score (>=6)			
Gleason score can range from 2-10. The higher the Gleason Score, the more likely that the cancer will grow and spread quickly. Scores of 6 (or less) describe cancer cells that look similar to normal cells and suggest that the cancer is likely to grow slowly. A score of 7 suggests an intermediate risk for aggressive cancer. Scores of 8 (or higher) describe cancers that are likely to spread more rapidly, these cancers are often referred to as poorly differentiated or high grade.			
Units: Subjects			
Gleason score = 6	1		
Gleason score = 7	10		
Gleason score = 8	5		
Gleason score = 9	7		
Gleason score = 10	2		
Gleason score = Missing	2		
Time since first prostate cancer diagnosis			
Time since first prostate cancer diagnosis is defined as (date of screening – date of first prostate cancer diagnosis + 1) / 30.4375.			
Units: Months			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Phase I: Dose Escalation Cohort 1
Reporting group description: Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 2
Reporting group description: Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 3A
Reporting group description: Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 3B
Reporting group description: Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 4B
Reporting group description: Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 4C
Reporting group description: Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 5C
Reporting group description: Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 5D
Reporting group description: Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	
Reporting group title	Phase I: Dose Escalation Cohort 6E
Reporting group description: Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)	
Subject analysis set title	Phase I: Dose Escalation Cohort 1 (Cycle 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I: Dose Escalation Cohort 1 (Cycle 1 at 100 mCi)	
Subject analysis set title	Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1 at 200 mCi)	
Subject analysis set title	Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1 at 300 mCi)	
Subject analysis set title	Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1 at 400 mCi)	
Subject analysis set title	Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1 at 500 mCi)	

Primary: Phase I: Incidence of dose limiting toxicities (DLTs) during first cycle of study treatment.

End point title	Phase I: Incidence of dose limiting toxicities (DLTs) during first cycle of study treatment.[1]

End point description:

A dose-limiting toxicity (DLT) was defined as any toxicity not attributable to the disease or disease-related processes under investigation, the time window for DLT assessment period was Cycle 1. To be considered a DLT, it was to be related to the IP (attributions: possible, probable, and definite) while fulfilling one of the following criteria as per the NCI Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0.

End point type	Primary

End point timeframe:

Up to 8 weeks after the first 177Lu-PSMA-R2 dose

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 analysis performed

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Number of Participants with Treatment Emergent Adverse Events (TEAEs)

End point title	Phase I: Number of Participants with Treatment Emergent Adverse Events (TEAEs)

End point description:

The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs) and Serious Adverse Event (TESAEs), through the monitoring of relevant clinical and laboratory safety parameters.

End point type	Secondary

End point timeframe:

From randomization till 30 days safety follow-up, assessed up to approximately 4 years

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants				
At least one TEAE	3	3	3	3
TEAE rel. to 68Ga-PSMA-R2	0	0	1	1
TEAE rel. to 177Lu-PSMA-R2	2	2	2	3
TEAE rel. to the study procedure	0	3	1	1
Serious TEAE	1	1	1	1
Serious TEAE rel. to 68Ga-PSMA-R2	0	0	0	0
Serious TEAE rel. to 177Lu-PSMA-R2	0	0	1	0
Serious TEAE rel. to the study procedure	0	0	0	0
TEAE leading to study discontinuation	1	0	0	0
Mild TEAE	3	3	3	3
Moderate TEAE	2	3	2	1
Severe TEAE	0	1	1	2
Life threatening TEAE	1	1	0	0
TEAE leading to death	1	0	0	0
At least one DLT	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants				
At least one TEAE	3	3	3	3
TEAE rel. to 68Ga-PSMA-R2	0	1	2	0
TEAE rel. to 177Lu-PSMA-R2	2	2	3	3
TEAE rel. to the study procedure	0	0	0	0
Serious TEAE	2	0	0	0
Serious TEAE rel. to 68Ga-PSMA-R2	0	0	0	0
Serious TEAE rel. to 177Lu-PSMA-R2	0	0	0	0
Serious TEAE rel. to the study procedure	0	0	0	0
TEAE leading to study discontinuation	0	0	0	0
Mild TEAE	3	3	3	3
Moderate TEAE	3	1	2	1
Severe TEAE	2	0	0	0

Life threatening TEAE	0	0	0	0
TEAE leading to death	0	0	0	0
At least one DLT	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
At least one TEAE	3			
TEAE rel. to 68Ga-PSMA-R2	0			
TEAE rel. to 177Lu-PSMA-R2	3			
TEAE rel. to the study procedure	1			
Serious TEAE	0			
Serious TEAE rel. to 68Ga-PSMA-R2	0			
Serious TEAE rel. to 177Lu-PSMA-R2	0			
Serious TEAE rel. to the study procedure	0			
TEAE leading to study discontinuation	0			
Mild TEAE	3			
Moderate TEAE	1			
Severe TEAE	0			
Life threatening TEAE	0			
TEAE leading to death	0			
At least one DLT	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Number of participants with an Objective Response Rate (ORR)

End point title	Phase I: Number of participants with an Objective Response Rate (ORR)

End point description:

The objective response rate (ORR) was defined as the proportion of participants with Best Overall Response (BOR) of Complete Response (CR) or Partial Response (PR), as assessed per RECIST 1.1 by the investigator.

End point type	Secondary

End point timeframe:

From date of randomization until date of progression or date of death from any cause, whichever comes first, assessed up to approximately 4 years

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants				
ORR in overall population	0	0	0	0
ORR in patients with visceral disease at Baseline	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants				
ORR in overall population	0	0	0	0
ORR in patients with visceral disease at Baseline	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
ORR in overall population	1			
ORR in patients with visceral disease at Baseline	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Duration of Response (DoR)

End point title	Phase I: Duration of Response (DoR)

End point description:

Duration of Response (DOR) according to RECIST v1.1 was defined as the time that measurement criteria were met for objective response (BOR of Complete Response (CR) or Partial Response (PR)) (whichever status was recorded first) until the first date of progression or death was documented.

End point type	Secondary

End point timeframe:

From first documented evidence of CR or PR (the response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to approximately 4 years

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[2] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

[3] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

[4] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

[5] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[6]	0[7]	0[8]	0[9]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[6] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

[7] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

[8] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

[9] - No participants with BOR of Complete Response (CR) or Partial Response (PR)

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Months				
median (confidence interval 95%)	2.63 (0 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 30

End point title	Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 30

End point description:

PSA response rate 30 was defined as the proportion of participants who had a greater or equal 30% in PSA from Baseline that was confirmed by a second PSA measurement 4 weeks later, as per Prostate Cancer Working Group 3 (PCWG3) criteria.

End point type	Secondary

End point timeframe:

Week 13 (12 weeks after the first 177Lu-PSMA-R2 injection)

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	1

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 50

End point title	Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 50

End point description:

PSA response rate 50 was defined as the proportion of participants who had a greater or equal 50% in PSA from Baseline that was confirmed by a second PSA measurement 4 weeks later, as per Prostate Cancer Working Group 3 (PCWG3) criteria.

End point type	Secondary

End point timeframe:

Week 13 (12 weeks after the first 177Lu-PSMA-R2 injection)

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Maximum plasma concentration (Cmax) of 177Lu-PSMA-R2

End point title	Phase I: Maximum plasma concentration (Cmax) of 177Lu-PSMA-R2

End point description:

Venous whole blood samples was collected in a subset of 18 patients (3 patients from each cohort testing a new dose strength) for activity-based pharmacokinetics characterization. Cmax was listed and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Day 1 (before the start of infusion, at the mid-point, and just before the end of infusion, then at post infusion at approximately 5, 15, 30 minutes, 1, 2, 4, 6, 8, 24, 40 (+/- 4 hours), 48 hours), Day 4 (+2 days) and Day 8 post end of infusion

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	0[10]	3
Units: ng/mL				
geometric mean (geometric coefficient	7.16 (± 46.9)	12.8 (± 33.8)	()	21.7 (± 31.2)

of variation)

Notes:

[10] - PK assessments done in 3 patients from each cohort testing a new dose strength

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	3	0[12]	3
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	21.9 (± 25.2)	()	32.8 (± 8.17)

Notes:

[11] - PK assessments done in 3 patients from each cohort testing a new dose strength

[12] - PK assessments done in 3 patients from each cohort testing a new dose strength

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	43.7 (± 41.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (AUCtlast) of 177Lu-PSMA-R2

End point title	Phase I: Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (AUCtlast) of 177Lu-PSMA-R2

End point description:

Venous whole blood samples was collected in a subset of 18 patients (3 patients from each cohort testing a new dose strength) for activity-based pharmacokinetics characterization. AUCtlast was listed and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Day 1 (before the start of infusion, at the mid-point, and just before the end of infusion, then at post infusion at approximately 5, 15, 30 minutes, 1, 2, 4, 6, 8, 24, 40 (+/- 4 hours), 48 hours), Day 4 (+2 days) and Day 8 post end of infusion

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	0[13]	3
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	21.3 (± 53.8)	36.3 (± 35.2)	()	85.9 (± 4.81)

Notes:

[13] - PK assessments done in 3 patients from each cohort testing a new dose strength

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[14]	3	0[15]	3
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	()	82.7 (± 39.5)	()	126 (± 32.7)

Notes:

[14] - PK assessments done in 3 patients from each cohort testing a new dose strength

[15] - PK assessments done in 3 patients from each cohort testing a new dose strength

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	207 (± 17.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Area under the serum concentration-time curve from time zero to (AUCinf) of 177Lu-PSMA-R2

End point title	Phase I: Area under the serum concentration-time curve from time zero to (AUCinf) of 177Lu-PSMA-R2

End point description:

Venous whole blood samples was collected in a subset of 18 patients (3 patients from each cohort testing a new dose strength) for activity-based pharmacokinetics characterization. AUCinf was listed and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Day 1 (before the start of infusion, at the mid-point, and just before the end of infusion, then at post infusion at approximately 5, 15, 30 minutes, 1, 2, 4, 6, 8, 24, 40 (+/- 4 hours), 48 hours), Day 4 (+2 days) and Day 8 post end of infusion

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	0[16]	3
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	21.3 (± 53.8)	37.9 (± 37.5)	()	86.6 (± 4.59)

Notes:

[16] - PK assessments done in 3 patients from each cohort testing a new dose strength

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[17]	3	0[18]	3
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	()	83.1 (± 39.8)	()	127 (± 32.7)

Notes:

[17] - PK assessments done in 3 patients from each cohort testing a new dose strength

[18] - PK assessments done in 3 patients from each cohort testing a new dose strength

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	207 (± 17.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Absorbed doses of 177Lu-PSMA-R2 by critical organs

End point title	Phase I: Absorbed doses of 177Lu-PSMA-R2 by critical organs

End point description:

Absorbed doses of 177Lu-PSMA-R2 were assessed by critical organs and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Days 1 through 8 post-treatment

End point values	Phase I: Dose Escalation Cohort 1 (Cycle 1)	Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1)	Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1)	Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	6	6	6
Units: Gy/GBq				
arithmetic mean (standard deviation)				
Adrenal Gland	0.0054 (± 0.00090)	0.062 (± 0.020)	0.010 (± 0.0037)	0.0083 (± 0.0019)
Bladder Wall	0.43 (± 0.029)	0.37 (± 0.036)	0.29 (± 0.067)	0.038 (± 0.052)
Bone Marrow	0.0087 (± 0.0038)	0.052 (± 0.016)	0.016 (± 0.0026)	0.011 (± 0.0042)
Brain	0.0014 (± 0.00080)	0.0044 (± 0.0017)	0.0025 (± 0.00078)	0.0023 (± 0.00052)
Colon, Left	0.17 (± 0.050)	0.37 (± 0.14)	0.61 (± 0.14)	0.38 (± 0.14)
Colon, Right	0.092 (± 0.026)	0.22 (± 0.084)	0.33 (± 0.075)	0.20 (± 0.076)
Esophagus	0.0019 (± 0.00041)	0.059 (± 0.019)	0.0044 (± 0.0021)	0.0037 (± 0.0013)
Eye	0.0012 (± 0.00040)	0.058 (± 0.018)	0.0032 (± 0.0016)	0.0028 (± 0.00096)
Gallbladder	0.0028 (± 0.00052)	0.061 (± 0.019)	0.0068 (± 0.0026)	0.0053 (± 0.00094)
Heart, Ventricular Wall	0.059 (± 0.047)	0.046 (± 0.015)	0.096 (± 0.046)	0.051 (± 0.031)
Kidney	0.025 (± 0.035)	0.15 (± 0.046)	0.34 (± 0.15)	0.28 (± 0.15)
Lacrimal Gland	0.060 (± 0.035)	0.096 (± 0.097)	0.096 (± 0.043)	0.069 (± 0.011)
Liver	0.020 (± 0.0055)	0.014 (± 0.0066)	0.032 (± 0.014)	0.026 (± 0.010)
Lung	0.0092 (± 0.00014)	0.017 (± 0.0054)	0.026 (± 0.019)	0.023 (± 0.019)
Osteogenic Cells	0.0056 (± 0.0022)	0.070 (± 0.022)	0.011 (± 0.0025)	0.0082 (± 0.0028)
Pancreas	0.0026 (± 0.00044)	0.062 (± 0.020)	0.0066 (± 0.0025)	0.0051 (± 0.00072)
Prostate Gland	0.0047 (± 0.00025)	0.064 (± 0.019)	0.0075 (± 0.0018)	0.0067 (± 0.00055)
Rectum	0.16 (± 0.047)	0.35 (± 0.14)	0.58 (± 0.13)	0.36 (± 0.14)
Salivary Gland	0.025 (± 0.010)	0.069 (± 0.028)	0.050 (± 0.021)	0.040 (± 0.011)
Small Intestine	0.16 (± 0.0040)	0.087 (± 0.029)	0.055 (± 0.013)	0.035 (± 0.011)
Spleen	0.012 (± 0.014)	0.048 (± 0.032)	0.030 (± 0.023)	0.080 (± 0.063)
Stomach	0.0020 (± 0.00042)	0.061 (± 0.019)	0.0049 (± 0.0022)	0.0041 (± 0.0010)
Testis	0.0019 (± 0.00037)	0.060 (± 0.019)	0.0037 (± 0.0016)	0.0034 (± 0.00094)
Thymus Gland	0.0018 (± 0.00039)	0.060 (± 0.019)	0.0042 (± 0.0021)	0.0034 (± 0.0013)
Thyroid Gland	0.066 (± 0.047)	0.057 (± 0.027)	0.090 (± 0.047)	0.12 (± 0.10)
Whole-body	0.0074 (± 0.00069)	0.065 (± 0.020)	0.013 (± 0.0037)	0.011 (± 0.00091)

End point values	Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: Gy/GBq				
arithmetic mean (standard deviation)				
Adrenal Gland	0.0087 (± 0.0024)			
Bladder Wall	0.36 (± 0.042)			
Bone Marrow	0.012 (± 0.0026)			
Brain	0.0027 (± 0.00078)			
Colon, Left	0.33 (± 0.12)			
Colon, Right	0.18 (± 0.063)			
Esophagus	0.0039 (± 0.0016)			
Eye	0.0029 (± 0.0015)			
Gallbladder	0.0055 (± 0.0019)			
Heart, Ventricular Wall	0.071 (± 0.037)			
Kidney	0.27 (± 0.14)			
Lacrimal Gland	0.094 (± 0.034)			
Liver	0.034 (± 0.014)			
Lung	0.020 (± 0.012)			
Osteogenic Cells	0.0088 (± 0.0019)			
Pancreas	0.0051 (± 0.0018)			
Prostate Gland	0.0066 (± 0.0015)			
Rectum	0.31 (± 0.11)			
Salivary Gland	0.051 (± 0.022)			
Small Intestine	0.031 (± 0.010)			
Spleen	0.091 (± 0.066)			
Stomach	0.0042 (± 0.0016)			
Testis	0.0035 (± 0.0015)			
Thymus Gland	0.0036 (± 0.0016)			
Thyroid Gland	0.12 (± 0.11)			
Whole-body	0.011 (± 0.0024)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Residence times of 177Lu-PSMA-R2 in normal organs

End point title	Phase I: Residence times of 177Lu-PSMA-R2 in normal organs

End point description:

Residence times of 177Lu-PSMA-R2 were assessed in normal organs and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Days 1 through 8 post-treatment

End point values	Phase I: Dose Escalation Cohort 1 (Cycle 1)	Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1)	Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1)	Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	6	6	6
Units: MBq-hr/MBq				
median (full range (min-max))				
Bladder	0.26 (0.14 to 0.59)	999 (999 to 999)	1.5 (0.63 to 2.4)	0.84 (0.32 to 0.89)
Body	5.6 (4.0 to 6.2)	51 (32 to 63)	8.7 (6.4 to 16)	7.1 (7.1 to 8.9)
Bone Marrow	0.12 (0.12 to 0.27)	0.12 (0.10 to 0.14)	0.30 (0.26 to 0.34)	0.17 (0.14 to 0.30)
Brain	0.026 (0.0082 to 0.033)	0.044 (0.020 to 0.053)	0.033 (0.029 to 0.053)	0.040 (0.027 to 0.041)
Heart, Ventricular Wall	0.17 (0.078 to 0.43)	0.15 (0.11 to 0.21)	0.28 (0.24 to 0.56)	0.16 (0.095 to 0.32)
Intestine	0.51 (0.45 to 0.58)	0.83 (0.44 to 0.90)	2.4 (1.3 to 6.4)	0.98 (0.89 to 1.8)
Kidney	0.92 (0.74 to 0.97)	0.48 (0.40 to 0.71)	1.1 (0.90 to 1.7)	0.90 (0.67 to 1.6)
Lacrimal Gland	0.0016 (0.0013 to 0.0036)	0.0019 (0.0010 to 0.0075)	0.0030 (0.0022 to 0.0052)	0.0025 (0.0021 to 0.0029)
Liver	0.42 (0.27 to 0.49)	0.22 (0.095 to 0.31)	0.48 (0.43 to 0.92)	0.44 (0.32 to 0.72)
Lung	0.12 (0.12 to 0.13)	0.20 (0.11 to 0.22)	0.29 (0.11 to 0.64)	0.19 (0.13 to 0.61)
Salivary Gland	0.024 (0.016 to 0.036)	0.050 (0.049 to 0.095)	0.039 (0.035 to 0.074)	0.038 (0.030 to 0.051)
Spleen	0.0055 (0.0050 to 0.048)	0.060 (0.031 to 0.13)	0.030 (0.023 to 0.092)	0.11 (0.039 to 0.26)

Thyroid Gland	0.015 (0.0047 to 0.027)	0.0091 (0.0085 to 0.019)	0.016 (0.014 to 0.034)	0.022 (0.0084 to 0.054)

End point values	Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: MBq-hr/MBq				
median (full range (min-max))				
Bladder	1.2 (0.46 to 2.9)			
Body	8.4 (6.3 to 11)			
Bone Marrow	0.22 (0.17 to 0.33)			
Brain	0.044 (0.022 to 0.058)			
Heart, Ventricular Wall	0.28 (0.11 to 0.42)			
Intestine	1.4 (0.61 to 2.6)			
Kidney	0.97 (0.66 to 1.9)			
Lacrimal Gland	0.0030 (0.0025 to 0.0058)			
Liver	0.68 (0.31 to 1.1)			
Lung	0.21 (0.10 to 0.50)			
Salivary Gland	0.048 (0.024 to 0.080)			
Spleen	0.15 (0.020 to 0.31)			
Thyroid Gland	0.020 (0.0065 to 0.076)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Mouth Dryness using Xerostomia Questionnaire

End point title	Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Mouth Dryness using Xerostomia Questionnaire

End point description:

The Xerostomia questionnaire is a questionnaire used to describe mouth dryness and its effects on daily life. It consists of 8 questions with each question score ranging from 0 ("never"/"none") to 10 ("worst"). The sum of the 8 scores produces a total score (score range from 0-80). A low score corresponds to a good quality of life while a high score means a poor quality of life due to the dry mouth.

End point type	Secondary

End point timeframe:
Baseline, Cycle 1 Day 1, Cycle 3 Day 85, Follow Up 1, Follow Up 2, Follow Up 3, Follow Up 4

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 3 Day 85 Change from Baseline	999 (± 999)	-4.0 (± 999)	4.7 (± 8.96)	-2.5 (± 9.19)
Follow Up 1 Change from Baseline	999 (± 999)	999 (± 999)	-1.0 (± 999)	0.5 (± 13.44)
Follow Up 2 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	-4.5 (± 6.36)
Follow Up 3 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	21.0 (± 999)
Follow Up 4 Change from Baseline	999 (± 999)	999 (± 999)	-1.0 (± 999)	999 (± 999)

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 3 Day 85 Change from Baseline	999 (± 999)	-8.0 (± 999)	14.0 (± 999)	999 (± 999)
Follow Up 1 Change from Baseline	6.0 (± 999)	-8.0 (± 999)	2.5 (± 4.95)	-2.3 (± 4.04)
Follow Up 2 Change from Baseline	0.0 (± 999)	18.0 (± 999)	-2.0 (± 999)	999 (± 999)
Follow Up 3 Change from Baseline	999 (± 999)	-7.0 (± 4.24)	999 (± 999)	999 (± 999)
Follow Up 4 Change from Baseline	999 (± 999)	999 (± 999)	16.0 (± 999)	999 (± 999)

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Change from Baseline	999 (± 999)			
Cycle 3 Day 85 Change from Baseline	-0.7 (± 3.06)			
Follow Up 1 Change from Baseline	2.3 (± 14.64)			
Follow Up 2 Change from Baseline	3.3 (± 8.50)			
Follow Up 3 Change from Baseline	4.7 (± 7.23)			
Follow Up 4 Change from Baseline	18.5 (± 26.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Eye Dryness using Xerophthalmia Questionnaire

End point title	Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Eye Dryness using Xerophthalmia Questionnaire

End point description:

The Xerophthalmia questionnaire is a questionnaire used to describe eye dryness and its effects on daily life. It consists of 3 questions. The first 2 questions scores range from 1 ("never") to 4 ("constantly") and the last question is a Yes/No question about previous dry eye diagnosis. The sum of the scores of the first 2 questions produces a total score (score range from 2-8). A low score corresponds to a good quality of life while a high score means a poor quality of life due to the dry eye.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Day 1, Cycle 3 Day 85, Follow Up 1, Follow Up 2, Follow Up 3, Follow Up 4

End point values	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 3 Day 85 Change from Baseline	999 (± 999)	-2.0 (± 999)	0.0 (± 0.00)	-1.0 (± 1.41)
Follow Up 1 Change from Baseline	999 (± 999)	999 (± 999)	-2.0 (± 999)	-0.5 (± 2.12)
Follow Up 2 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	-0.5 (± 2.12)
Follow Up 3 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	-2.0 (± 999)
Follow Up 4 Change from Baseline	999 (± 999)	999 (± 999)	-2.0 (± 999)	999 (± 999)

End point values	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Change from Baseline	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
Cycle 3 Day 85 Change from Baseline	999 (± 999)	1.0 (± 999)	1.0 (± 999)	999 (± 999)
Follow Up 1 Change from Baseline	0.0 (± 999)	0.0 (± 999)	1.5 (± 0.71)	-0.3 (± 0.58)

Follow Up 2 Change from Baseline	0.0 (± 999)	0.0 (± 999)	0.0 (± 999)	999 (± 999)
Follow Up 3 Change from Baseline	999 (± 999)	0.0 (± 0.00)	999 (± 999)	999 (± 999)
Follow Up 4 Change from Baseline	999 (± 999)	999 (± 999)	2.0 (± 999)	999 (± 999)

End point values	Phase I: Dose Escalation Cohort 6E			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Change from Baseline	999 (± 999)			
Cycle 3 Day 85 Change from Baseline	0.0 (± 0.00)			
Follow Up 1 Change from Baseline	-0.3 (± 0.58)			
Follow Up 2 Change from Baseline	0.0 (± 0.00)			
Follow Up 3 Change from Baseline	0.0 (± 0.00)			
Follow Up 4 Change from Baseline	0.0 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From informed consent signature through study completion reached at early termination date on 02-Jun-2022, assessed up to approximately 4 years.

Adverse event reporting additional description:

Consistent with EudraCTdisclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Cohort 3B: 3 cycles at 300 mCi
Reporting group description:	
Cohort 3B: 3 cycles at 300 mCi	
Reporting group title	Cohort 3A: 4 cycles at 200 mCi
Reporting group description:	
Cohort 3A: 4 cycles at 200 mCi	
Reporting group title	Cohort 2: 3 cycles at 200 mCi
Reporting group description:	
Cohort 2: 3 cycles at 200 mCi	
Reporting group title	Cohort 1: 3 cycles at 100 mCi
Reporting group description:	
Cohort 1: 3 cycles at 100 mCi	
Reporting group title	Cohort 5D: 2 cycles at 500 mCi
Reporting group description:	
Cohort 5D: 2 cycles at 500 mCi	
Reporting group title	Cohort 5C: 4 cycles at 400 mCi
Reporting group description:	
Cohort 5C: 4 cycles at 400 mCi	
Reporting group title	Cohort 4C: 3 cycles at 400 mCi
Reporting group description:	
Cohort 4C: 3 cycles at 400 mCi	
Reporting group title	Cohort 6E: 3 cycles at 500 mCi
Reporting group description:	
Cohort 6E: 3 cycles at 500 mCi	
Reporting group title	Cohort 4B: 4 cycles at 300 mCi
Reporting group description:	
Cohort 4B: 4 cycles at 300 mCi	

Serious adverse events	Cohort 3B: 3 cycles at 300 mCi	Cohort 3A: 4 cycles at 200 mCi	Cohort 2: 3 cycles at 200 mCi
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
number of deaths (all causes)	3	1	1

number of deaths resulting from adverse events	0	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Back pain			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 1: 3 cycles at 100 mCi	Cohort 5D: 2 cycles at 500 mCi	Cohort 5C: 4 cycles at 400 mCi
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Nervous system disorders			
Hypoaesthesia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Acute respiratory failure			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 4C: 3 cycles at 400 mCi	Cohort 6E: 3 cycles at 500 mCi	Cohort 4B: 4 cycles at 300 mCi
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
number of deaths (all causes)	2	0	3
number of deaths resulting from adverse events	0	0	0
Investigations			

Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 3B: 3 cycles at 300 mCi	Cohort 3A: 4 cycles at 200 mCi	Cohort 2: 3 cycles at 200 mCi
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infusion site coldness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Prostatic pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Amylase decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Blood chloride increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood creatine increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eosinophil count decreased			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Immature granulocyte percentage increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Immature granulocyte count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lipase decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Mean cell haemoglobin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Protein urine present			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary casts			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine analysis abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
White blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Lip injury			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood loss anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Xerophthalmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyschezia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oral pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

COVID-19			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Cohort 1: 3 cycles at 100 mCi	Cohort 5D: 2 cycles at 500 mCi	Cohort 5C: 4 cycles at 400 mCi
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Fatigue			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site coldness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Prostatic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Amylase decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood chloride increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood fibrinogen decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eosinophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Eosinophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immature granulocyte percentage increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immature granulocyte count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Mean cell haemoglobin increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Protein urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Red blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary casts			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urine analysis abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
White blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Lip injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood loss anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Xerophthalmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Frequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyschezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oral pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	2
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Coccydynia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 4C: 3 cycles at 400 mCi	Cohort 6E: 3 cycles at 500 mCi	Cohort 4B: 4 cycles at 300 mCi
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site coldness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Prostatic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Amylase decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Blood chloride increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood fibrinogen decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Eosinophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Eosinophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immature granulocyte percentage increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immature granulocyte count increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	3	4
Mean cell haemoglobin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Protein urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Red blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary casts			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine analysis abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	3
White blood cells urine positive			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Lip injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood loss anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Xerophthalmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyschezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Liver injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ingrowing nail			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Coccydynia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2018	Changes regarding secondary endpoint PSA response rate determination, treatment discontinuation, follow-up period testing, visit schedule variations, exclusion criteria, dosimetry analysis, safety dose-limiting toxicity determination and prohibited concomitant determination.
22 February 2018	No major changes from version 1.1. The changes in this version are mainly formatting changes and corrections of typographical errors.
02 July 2018	The main purpose of this amendment was to (A) include dosimetry, pharmacokinetics and imaging assessments in cohort 2 as well as all subsequent cohorts with a dose increase (B) move salivary gland scintigraphy from Day 1 to the Screening Period in order to allow clearance of radioactive tracer Tc99m and avoid Tc-99m's possible impact on dosimetry assessments.
29 April 2019	The main purpose of this amendment was to enhance the dose escalation algorithm in Phase-I to allow testing of more dosing schedules during the dose-escalation phase by increasing the strength as well as testing different cycles of 177Lu-PSMA-R2, to determine RP2D. The amendment also clarified and ensured alignment between the objectives and endpoints of both Phase I and Phase II. Certain endpoints were moved from exploratory to secondary for both Phase I and Phase II. Given the single arm design of Phase II, primary objective, was changed from assessment of rPFS to assessment of PSA reduction of 50% or higher compared to baseline and rPFS was moved to secondary endpoint. Due to its relevance for radioligand therapy Disease Control Rate (DCR), and PSA response of 30% or higher was added to the secondary endpoint for Phase II. Duration of Response (DoR), Objective Response Rate (ORR) was added as a secondary endpoint for both Phase I and Phase II. Statistical assumptions for Phase II was updated accordingly.
30 September 2019	Clarifications on specific sections of the study design and stopping guidelines were provided. Other administrative annotations were provided.

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 EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results.

Please use https://www.novctrd.com for complete trial results.

Notes: