



Clinical trial results:

A Randomized Phase 3 Study Comparing Cabazitaxel/Prednisone in Combination with Custirsen (OGX-011) to Cabazitaxel/Prednisone for Second-Line Chemotherapy in Men with Metastatic Castrate Resistant Prostate Cancer (AFFINITY)

Summary

EudraCT number	2012-001461-32
Trial protocol	GB HU CZ
Global end of trial date	15 July 2016

Results information

Result version number	v1 (current)
This version publication date	05 January 2017
First version publication date	05 January 2017

Trial information

Trial identification

Sponsor protocol code	OGX-011-12
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01578655
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OncoGenex Technologies, Inc.
Sponsor organisation address	19820 North Creek Parkway, Suite 201, Bothell, United States, 98011
Public contact	Chief Medical Officer, OncoGenex Technologies, Inc., 001 425-686-1500,
Scientific contact	Chief Medical Officer, OncoGenex Technologies, Inc., 001 425-686-1500,

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	15 July 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This Phase 3 study has been designed to confirm that adding custirsen to cabazitaxel/prednisone treatment can slow tumor progression and enhance survival outcomes compared to standard cabazitaxel/prednisone treatment in men with metastatic castrate resistant prostate cancer (CRPC).

The co-primary objectives for this study are based on determining whether the survival time distribution for applicable subjects randomized to the investigational arm (cabazitaxel/prednisone plus custirsen) is consistent with longer survival as compared to subjects randomized to the control arm (cabazitaxel/prednisone).

Subjects who were removed from study treatment for any reason other than disease progression (e.g., toxicity) were followed for documented disease progression and survival status. Once disease progression was documented, subjects entered a survival follow-up phase during which data was collected regarding further treatment for disease progression and the date of death.

Protection of trial subjects:

Each subject was provided an informed consent form that was reviewed and approved by the site's governing Institutional Review Board (IRB), Research Ethics Board (REB) or Ethics Committee (EC). The Principal Investigator (or designee) provided potential subjects with a verbal description of the study, including but not limited to, study purpose and study procedures, risks and benefits and answered all subject questions prior to signing the form.

Background therapy:

Cabazitaxel (25 mg/m²) was administered intravenously (IV) on Day 1 of each 21-day cycle.

Prednisone (10 mg orally [PO] per day) began on Day 1 of Cycle 1 and continued, at a minimum, through the completion of the final treatment cycle. Subjects who could not tolerate prednisone were not eligible for the study. If a subject was receiving more than the planned dose of 10 mg of prednisone per day (or steroid equivalent) at screening, the dose was reduced to 10 mg of prednisone per day prior to randomization.

Treatment cycles continued until disease progression, unacceptable toxicity, or completion of 10 cycles.

Evidence for comparator: -

Actual start date of recruitment	28 August 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 50
Country: Number of subjects enrolled	Canada: 83
Country: Number of subjects enrolled	France: 120

Country: Number of subjects enrolled	United Kingdom: 63
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Russian Federation: 133
Country: Number of subjects enrolled	United States: 143
Worldwide total number of subjects	635
EEA total number of subjects	226

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)	196
From 65 to 84 years	435
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening evaluations occurred in a period of up to 28 days (+3 days) prior to randomization.

Period 1

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

Blinding implementation details:

Because this trial was designed as an open-label trial, a blinding plan was implemented in order to minimize the chance of Sponsor decisions being affected by knowledge of the arm assignment of individual subjects, knowledge of the results from the secondary outcome, or accumulating survival data.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Prednisone/Cabazitaxel
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Arm description:

Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Arm type	No intervention
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No investigational medicinal product assigned in this arm

Arm title	Prednisone/Cabazitaxel + Custirsen
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Arm description:

Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles. Custirsen administered as 3 loading doses (640 mg IV each) within 9 days, followed by weekly custirsen (640 mg IV) during each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Arm type	Experimental
Investigational medicinal product name	custirsen sodium
Investigational medicinal product code	OGX-011
Other name	TV-1011
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Custirsen administered as 3 loading doses (640 mg IV each) within 9 days, followed by weekly custirsen (640 mg IV) during each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Number of subjects in period 1	Prednisone/Cabazitaxel	Prednisone/Cabazitaxel + Custirsen
Started	318	317
Received at Least 1 Dose of Study Drug	312	315
Entered Chemotherapy Period	312	306
Completed 10 Cycles of Chemotherapy	129 ^[1]	105 ^[2]
Entered Off-Treatment Follow-up	150 ^[3]	142 ^[4]
Entered Survival Follow-up	254 ^[5]	266
Completed	267	263
Not completed	51	54
Consent withdrawn by subject	5	1
Not specified	1	1
Study terminated by sponsor	45	51
Lost to follow-up	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects could have entered follow-up periods without completing all 10 cycles of chemotherapy.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects could have entered follow-up periods without completing all 10 cycles of chemotherapy.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects could have entered follow-up periods without completing all 10 cycles of chemotherapy.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects could have entered follow-up periods without completing all 10 cycles of chemotherapy.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects could have entered follow-up periods without completing all 10 cycles of chemotherapy.

Baseline characteristics

Reporting groups

Reporting group title	Prednisone/Cabazitaxel
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Reporting group description:

Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Reporting group title	Prednisone/Cabazitaxel + Custirsen
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Reporting group description:

Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles. Custirsen administered as 3 loading doses (640 mg IV each) within 9 days, followed by weekly custirsen (640 mg IV) during each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Reporting group values	Prednisone/Cabazitaxel	Prednisone/Cabazitaxel + Custirsen	Total
Number of subjects	318	317	635
Age, Customized Units: Participants			
≤ 65 years	117	109	226
> 65 years	201	208	409
Age Continuous Units: years			
least squares mean	67.7	67.8	
standard deviation	± 7.5	± 7.5	-
Gender, Male/Female Units: Participants			
Female	0	0	0
Male	318	317	635

End points

End points reporting groups

Reporting group title	Prednisone/Cabazitaxel
Reporting group description: Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m ² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.	
Reporting group title	Prednisone/Cabazitaxel + Custirsen
Reporting group description: Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m ² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles. Custirsen administered as 3 loading doses (640 mg IV each) within 9 days, followed by weekly custirsen (640 mg IV) during each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.	
Subject analysis set title	Prednisone/Cabazitaxel: Poor Prognosis Subgroup
Subject analysis set type	Sub-group analysis
Subject analysis set description: Prednisone (10 mg PO) is administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m ² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.	
Subject analysis set title	Prednisone/Cabazitaxel + Custirsen: Poor Prognosis Subgroup
Subject analysis set type	Sub-group analysis
Subject analysis set description: Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m ² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles. Custirsen administered as 3 loading doses (640 mg IV each) within 9 days, followed by weekly custirsen (640 mg IV) during each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.	

Primary: Overall Survival: Kaplan Meier Analysis

End point title	Overall Survival: Kaplan Meier Analysis
End point description: Overall survival time was defined as the number of days from the date of randomization until the date of death from any cause. Subjects who did not achieve the event (death) at the time of the analysis or who dropped out before completing the survival follow-up period were censored at the date they were last known to be alive (i.e., right censored). Partial or missing dates of death or last contact were imputed.	
End point type	Primary
End point timeframe: From randomization to death or last known date alive (up to 1382 days for Prednisone/Cabazitaxel arm and up to 1228 days for Prednisone/Cabazitaxel + Custirsen arm)	

End point values	Prednisone/Cabazitaxel	Prednisone/Cabazitaxel + Custirsen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	317		
Units: days				
median (confidence interval 95%)	409 (366 to 464)	431 (384 to 487)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Prednisone/Cabazitaxel + Custirsen v Prednisone/Cabazitaxel
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.264
Method	one-sided Score test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.946
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.796
upper limit	1.124

Primary: Overall Survival in the Poor-Prognosis Patient Population: Kaplan Meier Analysis

End point title	Overall Survival in the Poor-Prognosis Patient Population: Kaplan Meier Analysis
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End point description:

Overall survival time was defined as the number of days from the date of randomization until the date of death from any cause. Subjects who did not achieve the event (death) at the time of the analysis or who dropped out before completing the survival follow-up period were censored at the date they were last known to be alive (i.e., right censored). Partial or missing dates of death or last contact were imputed.

The following criteria, based on prognosis variables collected on or prior to the date of randomization, were used to classify subjects in the 'all randomized' analysis set as poor, good, or indeterminate prognosis:

1. Karnofsky performance status $\leq 80\%$
2. Presence of liver metastasis
3. LDH ≥ 360 U/L
4. Hemoglobin < 120 g/L
5. PSA ≥ 150 mg/L

To be classified as poor prognosis, subjects must have met at least 2 of the above prognostic criteria. For each prognostic variable, the value collected on or just prior to the date of randomization was evaluated.

End point type	Primary
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End point timeframe:

From randomization to death or last known date alive (up to 1056 days for Prednisone/Cabazitaxel arm and up to 887 days for Prednisone/Cabazitaxel + Custirsen arm)

End point values	Prednisone/Cabazitaxel: Poor Prognosis Subgroup	Prednisone/Cabazitaxel + Custirsen: Poor Prognosis Subgroup		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	197	195		
Units: days				
median (confidence interval 95%)	333 (252 to 378)	337 (282 to 406)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Prednisone/Cabazitaxel: Poor Prognosis Subgroup v Prednisone/Cabazitaxel + Custirsen: Poor Prognosis Subgroup
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235
Method	one-sided Score test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.727
upper limit	1.158

Secondary: Number of Subjects With 'Alive Without Event' Status at Day 140

End point title	Number of Subjects With 'Alive Without Event' Status at Day 140
End point description: Subjects who achieved a milestone Day 140 status of Alive Without Event. 'Yes' = alive and progression-free at Day 140; 'No' = death or disease progression on or before Day 140 or missing the Day 140 assessment.	
End point type	Secondary
End point timeframe: Day 140 (within the window of Day 125 to 155 post-randomization)	

End point values	Prednisone/Cabazitaxel	Prednisone/Cabazitaxel + Custirsen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	317		
Units: subjects				
number (not applicable)				

Yes	149	154		
No	169	163		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Prednisone/Cabazitaxel v Prednisone/Cabazitaxel + Custirsen
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3199 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.927
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.674
upper limit	1.274

Notes:

[1] - Based on one-sided Cochran-Mantel-Haenszel test controlling for stratification factors.

Secondary: Number of Subjects With 'Alive Without Event' Status at Day 140 in the Poor Prognosis Patient Population

End point title	Number of Subjects With 'Alive Without Event' Status at Day 140 in the Poor Prognosis Patient Population
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End point description:

Subjects who achieved a milestone Day 140 status of Alive Without Event. 'Yes' = alive and progression-free at Day 140; 'No' = death or disease progression on or before Day 140 or missing the Day 140 assessment.

The following criteria, based on prognosis variables collected on or prior to the date of randomization, were used to classify subjects in the 'all randomized' analysis set as poor, good, or indeterminate prognosis:

1. Karnofsky performance status $\leq 80\%$
2. Presence of liver metastasis
3. LDH ≥ 360 U/L
4. Hemoglobin < 120 g/L
5. PSA ≥ 150 mg/L

To be classified as poor prognosis, subjects must have met at least 2 of the above prognostic criteria. For each prognostic variable, the value collected on or just prior to the date of randomization was evaluated.

End point type	Secondary
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End point timeframe:

Day 140 (within the window of Day 125 to 155 post-randomization)

End point values	Prednisone/Cabazitaxel: Poor Prognosis Subgroup	Prednisone/Cabazitaxel + Custirsen: Poor Prognosis Subgroup		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	197	195		
Units: subjects				
number (not applicable)				
Yes	76	83		
No	121	112		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Prednisone/Cabazitaxel: Poor Prognosis Subgroup v Prednisone/Cabazitaxel + Custirsen: Poor Prognosis Subgroup
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2006 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.841
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.558
upper limit	1.268

Notes:

[2] - Based on one-sided Cochran-Mantel-Haenszel test controlling for stratification factors.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to last dose plus 30 days: 31 to 257 days for Prednisone/Cabazitaxel arm and 31 to 277 days for Prednisone/Cabazitaxel + Custirsen arm.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.1
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Reporting groups

Reporting group title	Prednisone/Cabazitaxel + Custirsen
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Reporting group description:

Prednisone (10 mg PO) administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m² IV) administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles. Custirsen administered as 3 loading doses (640 mg IV each) within 9 days, followed by weekly custirsen (640 mg IV) during each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Reporting group title	Prednisone/Cabazitaxel
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Reporting group description:

Prednisone (10 mg PO) is administered daily until disease progression, unacceptable toxicity, or completion of 10 cycles. Cabazitaxel (25 mg/m² IV) is administered on Day 1 of each 21-day cycle until disease progression, unacceptable toxicity, or completion of 10 cycles.

Serious adverse events	Prednisone/Cabazitaxel + Custirsen	Prednisone/Cabazitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	155 / 315 (49.21%)	132 / 312 (42.31%)	
number of deaths (all causes)	12	15	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			

subjects affected / exposed	3 / 315 (0.95%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyosarcoma			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative disorder			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 315 (0.63%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 315 (0.32%)	4 / 312 (1.28%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous stenosis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 315 (0.32%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter thrombosis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	2 / 315 (0.63%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Gait disturbance			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			

subjects affected / exposed	1 / 315 (0.32%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	2 / 315 (0.63%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	10 / 315 (3.17%)	3 / 312 (0.96%)	
occurrences causally related to treatment / all	2 / 10	2 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malaise			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 315 (0.32%)	3 / 312 (0.96%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	11 / 315 (3.49%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	10 / 13	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 315 (0.32%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal swelling			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 315 (0.32%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cough			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 315 (0.63%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	7 / 315 (2.22%)	8 / 312 (2.56%)	
occurrences causally related to treatment / all	4 / 7	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary oedema			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory failure			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			
Confusional state			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	2 / 315 (0.63%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Cervical vertebral fracture			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	2 / 315 (0.63%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fat embolism			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation injury			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal compression fracture			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subcutaneous haematoma			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	5 / 315 (1.59%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	2 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 315 (0.63%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Myocardial infarction			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cauda equina syndrome			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial neuropathy			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			

subjects affected / exposed	2 / 315 (0.63%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 315 (0.32%)	4 / 312 (1.28%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypoxic encephalopathy			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensorimotor neuropathy			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	6 / 315 (1.90%)	4 / 312 (1.28%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 315 (0.32%)	4 / 312 (1.28%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 315 (6.03%)	12 / 312 (3.85%)	
occurrences causally related to treatment / all	22 / 24	13 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	13 / 315 (4.13%)	9 / 312 (2.88%)	
occurrences causally related to treatment / all	15 / 15	9 / 9	
deaths causally related to treatment / all	1 / 1	1 / 1	
Leukopenia			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	7 / 315 (2.22%)	12 / 312 (3.85%)	
occurrences causally related to treatment / all	7 / 7	11 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 315 (0.32%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloedema			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Photophobia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia obstructive			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 315 (0.63%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	0 / 2	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 315 (0.63%)	3 / 312 (0.96%)	
occurrences causally related to treatment / all	0 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	10 / 315 (3.17%)	12 / 312 (3.85%)	
occurrences causally related to treatment / all	11 / 11	12 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 315 (0.63%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Irritable bowel syndrome			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 315 (0.95%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	2 / 3	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sigmoiditis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	9 / 315 (2.86%)	9 / 312 (2.88%)	
occurrences causally related to treatment / all	9 / 10	9 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic lesion			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder obstruction			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dysuria			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	15 / 315 (4.76%)	15 / 312 (4.81%)	
occurrences causally related to treatment / all	5 / 17	5 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage urinary tract			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 315 (0.63%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incontinence			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	1 / 315 (0.32%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	3 / 315 (0.95%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	3 / 3	2 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
Renal impairment			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric dilation			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	2 / 315 (0.63%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	9 / 315 (2.86%)	5 / 312 (1.60%)	
occurrences causally related to treatment / all	1 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelocaliectasis			
subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 315 (0.63%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	7 / 315 (2.22%)	8 / 312 (2.56%)	
occurrences causally related to treatment / all	1 / 7	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	6 / 315 (1.90%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	2 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 315 (0.32%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central line infection			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Escherichia bacteraemia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	0 / 315 (0.00%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	3 / 315 (0.95%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	2 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			

subjects affected / exposed	4 / 315 (1.27%)	2 / 312 (0.64%)	
occurrences causally related to treatment / all	4 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 315 (1.27%)	9 / 312 (2.88%)	
occurrences causally related to treatment / all	5 / 5	5 / 10	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pneumonia bacterial			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia escherichia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 315 (0.63%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	6 / 315 (1.90%)	7 / 312 (2.24%)	
occurrences causally related to treatment / all	1 / 6	6 / 7	
deaths causally related to treatment / all	0 / 1	2 / 2	
Staphylococcal sepsis			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	8 / 315 (2.54%)	4 / 312 (1.28%)	
occurrences causally related to treatment / all	8 / 8	5 / 5	
deaths causally related to treatment / all	4 / 4	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	14 / 315 (4.44%)	10 / 312 (3.21%)	
occurrences causally related to treatment / all	6 / 15	10 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	8 / 315 (2.54%)	8 / 312 (2.56%)	
occurrences causally related to treatment / all	8 / 9	5 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 315 (0.32%)	1 / 312 (0.32%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Prednisone/Cabazitaxel + Custirsen	Prednisone/Cabazitaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	312 / 315 (99.05%)	295 / 312 (94.55%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	16 / 315 (5.08%)	5 / 312 (1.60%)	
occurrences (all)	16	6	
Hypotension			
subjects affected / exposed	27 / 315 (8.57%)	16 / 312 (5.13%)	
occurrences (all)	36	17	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	75 / 315 (23.81%)	58 / 312 (18.59%)	
occurrences (all)	225	108	
Chills			
subjects affected / exposed	82 / 315 (26.03%)	5 / 312 (1.60%)	
occurrences (all)	101	5	
Fatigue			
subjects affected / exposed	136 / 315 (43.17%)	127 / 312 (40.71%)	
occurrences (all)	290	242	
Mucosal inflammation			
subjects affected / exposed	9 / 315 (2.86%)	18 / 312 (5.77%)	
occurrences (all)	11	21	
Oedema peripheral			
subjects affected / exposed	44 / 315 (13.97%)	36 / 312 (11.54%)	
occurrences (all)	59	43	
Pyrexia			
subjects affected / exposed	73 / 315 (23.17%)	20 / 312 (6.41%)	
occurrences (all)	105	23	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	34 / 315 (10.79%)	24 / 312 (7.69%)	
occurrences (all)	39	27	
Dyspnoea			
subjects affected / exposed	53 / 315 (16.83%)	39 / 312 (12.50%)	
occurrences (all)	82	45	

Psychiatric disorders			
Insomnia			
subjects affected / exposed	36 / 315 (11.43%)	26 / 312 (8.33%)	
occurrences (all)	39	32	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	19 / 315 (6.03%)	7 / 312 (2.24%)	
occurrences (all)	27	10	
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 315 (5.08%)	12 / 312 (3.85%)	
occurrences (all)	25	14	
Blood creatinine increased			
subjects affected / exposed	20 / 315 (6.35%)	8 / 312 (2.56%)	
occurrences (all)	28	9	
Weight decreased			
subjects affected / exposed	73 / 315 (23.17%)	42 / 312 (13.46%)	
occurrences (all)	105	61	
Nervous system disorders			
Dizziness			
subjects affected / exposed	47 / 315 (14.92%)	21 / 312 (6.73%)	
occurrences (all)	63	22	
Dysgeusia			
subjects affected / exposed	58 / 315 (18.41%)	36 / 312 (11.54%)	
occurrences (all)	91	63	
Headache			
subjects affected / exposed	34 / 315 (10.79%)	33 / 312 (10.58%)	
occurrences (all)	56	40	
Neuropathy peripheral			
subjects affected / exposed	23 / 315 (7.30%)	27 / 312 (8.65%)	
occurrences (all)	31	36	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	140 / 315 (44.44%)	109 / 312 (34.94%)	
occurrences (all)	376	255	
Leukopenia			

subjects affected / exposed	23 / 315 (7.30%)	16 / 312 (5.13%)	
occurrences (all)	53	48	
Neutropenia			
subjects affected / exposed	70 / 315 (22.22%)	59 / 312 (18.91%)	
occurrences (all)	154	113	
Thrombocytopenia			
subjects affected / exposed	56 / 315 (17.78%)	28 / 312 (8.97%)	
occurrences (all)	119	71	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	50 / 315 (15.87%)	27 / 312 (8.65%)	
occurrences (all)	70	35	
Constipation			
subjects affected / exposed	89 / 315 (28.25%)	78 / 312 (25.00%)	
occurrences (all)	147	118	
Abdominal pain upper			
subjects affected / exposed	16 / 315 (5.08%)	15 / 312 (4.81%)	
occurrences (all)	19	20	
Diarrhoea			
subjects affected / exposed	138 / 315 (43.81%)	130 / 312 (41.67%)	
occurrences (all)	336	280	
Dyspepsia			
subjects affected / exposed	18 / 315 (5.71%)	19 / 312 (6.09%)	
occurrences (all)	27	27	
Nausea			
subjects affected / exposed	143 / 315 (45.40%)	128 / 312 (41.03%)	
occurrences (all)	247	230	
Vomiting			
subjects affected / exposed	100 / 315 (31.75%)	74 / 312 (23.72%)	
occurrences (all)	191	128	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	22 / 315 (6.98%)	7 / 312 (2.24%)	
occurrences (all)	27	7	
Alopecia			

subjects affected / exposed occurrences (all)	13 / 315 (4.13%) 13	16 / 312 (5.13%) 18	
Rash subjects affected / exposed occurrences (all)	16 / 315 (5.08%) 20	4 / 312 (1.28%) 4	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	16 / 315 (5.08%) 20	16 / 312 (5.13%) 17	
Haematuria subjects affected / exposed occurrences (all)	59 / 315 (18.73%) 80	57 / 312 (18.27%) 81	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	26 / 315 (8.25%) 31	43 / 312 (13.78%) 68	
Back pain subjects affected / exposed occurrences (all)	53 / 315 (16.83%) 67	44 / 312 (14.10%) 68	
Bone pain subjects affected / exposed occurrences (all)	60 / 315 (19.05%) 72	43 / 312 (13.78%) 60	
Muscle spasms subjects affected / exposed occurrences (all)	19 / 315 (6.03%) 25	23 / 312 (7.37%) 35	
Myalgia subjects affected / exposed occurrences (all)	26 / 315 (8.25%) 33	9 / 312 (2.88%) 14	
Muscular weakness subjects affected / exposed occurrences (all)	17 / 315 (5.40%) 25	20 / 312 (6.41%) 27	
Pain in extremity subjects affected / exposed occurrences (all)	43 / 315 (13.65%) 57	23 / 312 (7.37%) 29	
Infections and infestations			

Urinary tract infection subjects affected / exposed occurrences (all)	37 / 315 (11.75%) 48	34 / 312 (10.90%) 38	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	100 / 315 (31.75%) 168	65 / 312 (20.83%) 101	
Dehydration subjects affected / exposed occurrences (all)	20 / 315 (6.35%) 24	13 / 312 (4.17%) 15	
Hypokalaemia subjects affected / exposed occurrences (all)	33 / 315 (10.48%) 50	12 / 312 (3.85%) 22	
Hypocalcaemia subjects affected / exposed occurrences (all)	24 / 315 (7.62%) 41	17 / 312 (5.45%) 43	
Hypophosphataemia subjects affected / exposed occurrences (all)	17 / 315 (5.40%) 25	15 / 312 (4.81%) 26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2015	<p>Changes to the protocol included:</p> <ul style="list-style-type: none">· Addition of a co-primary endpoint, which would allow prospective evaluation of a survival benefit specific to patients with poor prognostic disease.· Addition a second futility analysis and an interim efficacy analysis· Transfer of full sponsorship for this study to OncoGenex and remove Teva identifier (previously shared sponsorship).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported