Clinical trial results:
A Phase 3b, Multi-center, Open-label Trial to Evaluate the Long Term Safety of Immediate-release Tolvaptan (OPC-41061, 30 mg to 120 mg/day, Split Dose) in Subjects With Autosomal Dominant Polycystic Kidney Disease

Summary

EudraCT number	2014-001516-19
Trial protocol	GB IT SE NL BE PL ES CZ HU DK
Global end of trial date	09 November 2018

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019

Trial information

Trial identification

Sponsor protocol code	156-13-211

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02251275
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Otsuka Pharmaceutical Development & Commercialization, Inc.
Sponsor organisation address	2440 Research Boulevard, Rockville, MD, United States, 20850,
Public contact	Global Clinical Development, Otsuka Pharmaceutical Development & Commercialization, Inc., +1-609 524-6788, clinicaltransparency@otsuka-us.com
Scientific contact	Global Clinical Development, Otsuka Pharmaceutical Development & Commercialization, Inc., +1-609 524-6788, clinicaltransparency@otsuka-us.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	05 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2018
Global end of trial reached?	Yes
Global end of trial date	09 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the trial was to evaluate and describe the long term safety of tolvaptan in participants with autosomal dominant polycystic kidney disease (ADPKD).

Protection of trial subjects:

This trial was conducted in accordance with International Council on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which the trial was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2015
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	Argentina: 45
Country: Number of subjects enrolled	Australia: 59
Country: Number of subjects enrolled	Belgium: 90
Country: Number of subjects enrolled	Canada: 62
Country: Number of subjects enrolled	Czech Republic: 26
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Germany: 174
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Israel: 30
Country: Number of subjects enrolled	Italy: 91
Country: Number of subjects enrolled	Netherlands: 66
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Poland: 83
Country: Number of subjects enrolled	Romania: 29
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	South Africa: 20
Country: Number of subjects enrolled	Spain: 55
Country: Number of subjects enrolled	Sweden: 17
Country: Number of subjects enrolled	United Kingdom: 116
Country: Number of subjects enrolled	United States: 804

Worldwide total number of subjects	1803
EEA total number of subjects	775

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)	1773
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible participants could enroll into Trial 156-13-211 after completing follow-up visit(s) of their previous trial (156-13-210, 156-08-271, 156-04-251, or 156-09-290).

Pre-assignment

Screening details:

One participant screened, but withdrew consent on the same day (prior to study drug treatment) and is not included in the study data.
Starting doses depended on the participant's previous trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tolvaptan (From 156-13-210: Tolvaptan)

Arm description:

Participants were previously treated with tolvaptan in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 milligrams (mg) with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Arm type	Experimental
Investigational medicinal product name	tolvaptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The dose regimens used in this trial are 15/15 mg, 30/15 mg, 45/15 mg, 60/30 mg, and 90/30 mg. All doses were administered orally.

Arm title	Tolvaptan (From 156-13-210: Placebo)

Arm description:

Participants were previously treated with placebo in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Arm type	Experimental
Investigational medicinal product name	tolvaptan
Investigational medicinal product code	OPC-41061
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The dose regimens used in this trial were 15/15 mg, 30/15 mg, 45/15 mg, 60/30 mg, and 90/30 mg. All doses were administered orally.

Arm title	Tolvaptan (From 156-08-271: Tolvaptan)

Arm description:

Participants were previously treated with tolvaptan in Trial 156-08-271. Participants retained the last dose level of tolvaptan received in the trial (45/15 mg, 60/30 mg, or 90/30 mg) and started at that same dose in Trial 156-13-211.

Arm type	Experimental

Investigational medicinal product name	tolvaptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The dose regimens used in this trial are 15/15 mg, 30/15 mg, 45/15 mg, 60/30 mg, and 90/30 mg. All doses were administered orally.

Arm title	Tolvaptan (From Other: Tolvaptan)

Arm description:

Participants were previously treated with tolvaptan in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Arm type	Experimental
Investigational medicinal product name	tolvaptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The dose regimens used in this trial are 15/15 mg, 30/15 mg, 45/15 mg, 60/30 mg, and 90/30 mg. All doses were administered orally.

Arm title	Tolvaptan (From Other: Placebo)

Arm description:

Participants were previously treated with placebo in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Arm type	Experimental
Investigational medicinal product name	tolvaptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The dose regimens used in this trial are 15/15 mg, 30/15 mg, 45/15 mg, 60/30 mg, and 90/30 mg. All doses were administered orally.

Number of subjects in period 1	Tolvaptan (From 156-13-210: Tolvaptan)	Tolvaptan (From 156-13-210: Placebo)	Tolvaptan (From 156-08-271: Tolvaptan)
Started	506	570	718
Received at Least 1 Dose of Study Drug	505	569	717
Completed	434	423	624
Not completed	72	147	94
Physician decision	19	30	26
Consent withdrawn by subject	25	51	35
Adverse event, non-fatal	23	60	28
Protocol Deviation	-	-	1
Lost to follow-up	5	6	4

Number of subjects in period 1	Tolvaptan (From Other: Tolvaptan)	Tolvaptan (From Other: Placebo)
Started	6	3
Received at Least 1 Dose of Study Drug	6	3
Completed	5	2
Not completed	1	1
Physician decision	-	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	-
Protocol Deviation	-	-
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Tolvaptan (From 156-13-210: Tolvaptan)
Reporting group description:	
Participants were previously treated with tolvaptan in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 milligrams (mg) with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	
Reporting group title	Tolvaptan (From 156-13-210: Placebo)
Reporting group description:	
Participants were previously treated with placebo in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	
Reporting group title	Tolvaptan (From 156-08-271: Tolvaptan)
Reporting group description:	
Participants were previously treated with tolvaptan in Trial 156-08-271. Participants retained the last dose level of tolvaptan received in the trial (45/15 mg, 60/30 mg, or 90/30 mg) and started at that same dose in Trial 156-13-211.	
Reporting group title	Tolvaptan (From Other: Tolvaptan)
Reporting group description:	
Participants were previously treated with tolvaptan in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	
Reporting group title	Tolvaptan (From Other: Placebo)
Reporting group description:	
Participants were previously treated with placebo in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	

Reporting group values	Tolvaptan (From 156-13-210: Tolvaptan)	Tolvaptan (From 156-13-210: Placebo)	Tolvaptan (From 156-08-271: Tolvaptan)
Number of subjects	506	570	718
Age categorical			
Units:			
Age continuous			
Units: Years			
arithmetic mean	48.9	48.6	45.5
standard deviation	± 8.1	± 8.0	± 7.8
Gender categorical			
Units: Subjects			
Female	234	290	343
Male	272	280	375
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	3	0	0
Asian	16	16	10
Native Hawaiian or Other Pacific Islander	1	0	2
Black or African American	19	23	6
White	461	525	694
More than one race	0	0	0

Unknown or Not Reported	6	6	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	27	25	49
Not Hispanic or Latino	479	545	669
Unknown or Not Reported	0	0	0

Reporting group values	Tolvaptan (From Other: Tolvaptan)	Tolvaptan (From Other: Placebo)	Total
Number of subjects	6	3	1803
Age categorical Units:			
Age continuous Units: Years			
arithmetic mean	41.2	47.0	
standard deviation	± 11.4	± 2.6	-
Gender categorical Units: Subjects			
Female	5	2	874
Male	1	1	929
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	3
Asian	0	0	42
Native Hawaiian or Other Pacific Islander	0	0	3
Black or African American	0	0	48
White	6	3	1689
More than one race	0	0	0
Unknown or Not Reported	0	0	18
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	102
Not Hispanic or Latino	5	3	1701
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Tolvaptan (From 156-13-210: Tolvaptan)
Reporting group description:	
Participants were previously treated with tolvaptan in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 milligrams (mg) with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	
Reporting group title	Tolvaptan (From 156-13-210: Placebo)
Reporting group description:	
Participants were previously treated with placebo in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	
Reporting group title	Tolvaptan (From 156-08-271: Tolvaptan)
Reporting group description:	
Participants were previously treated with tolvaptan in Trial 156-08-271. Participants retained the last dose level of tolvaptan received in the trial (45/15 mg, 60/30 mg, or 90/30 mg) and started at that same dose in Trial 156-13-211.	
Reporting group title	Tolvaptan (From Other: Tolvaptan)
Reporting group description:	
Participants were previously treated with tolvaptan in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	
Reporting group title	Tolvaptan (From Other: Placebo)
Reporting group description:	
Participants were previously treated with placebo in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.	

Primary: Number Of Participants Reporting Treatment-Emergent Adverse Events (TEAEs)

End point title	Number Of Participants Reporting Treatment-Emergent Adverse Events (TEAEs)[1]
End point description:	
An adverse event (AE) was as any untoward medical occurrence associated with the use of an investigational medicinal product (IMP), whether or not considered IMP related. A TEAE was an AE that started after trial drug treatment; or if the event was continuous from baseline and was serious, related to IMP, or resulted in death, discontinuation, interruption or reduction of trial therapy. A serious TEAE included any event that resulted in: death, life-threatening, persistent or significant incapacity, substantial disruption of ability to conduct normal life functions, required inpatient hospitalization, prolonged hospitalization, congenital anomaly/birth defect, or other medically significant events as per medical judgment, that jeopardized the participant and that required medical or surgical intervention. A severe TEAE was an inability to work or perform normal daily activity. A summary of serious and all other non-serious TEAEs, regardless of causality, is located in the AE section.	
End point type	Primary
End point timeframe:	
Baseline through end of treatment (up to 42 months) and follow-up 7 days posttreatment (+ 7 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analyses were planned.

End point values	Tolvaptan (From 156-13-210: Tolvaptan)	Tolvaptan (From 156-13-210: Placebo)	Tolvaptan (From 156-08-271: Tolvaptan)	Tolvaptan (From Other: Tolvaptan)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	505	569	717	6
Units: participants				
number (not applicable)				
Participants with TEAEs	473	531	640	6
Participants with serious TEAEs	87	96	103	1
Participants with severe TEAEs	74	78	83	2
Discontinued due to TEAEs	33	65	38	0
Deaths	1	5	3	0

End point values	Tolvaptan (From Other: Placebo)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
number (not applicable)				
Participants with TEAEs	3			
Participants with serious TEAEs	2			
Participants with severe TEAEs	1			
Discontinued due to TEAEs	1			
Deaths	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through end of treatment (up to 42 months) and follow-up 7 days posttreatment (+ 7 days)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Tolvaptan (From 156-13-210: Tolvaptan)

Reporting group description:

Participants were previously treated with tolvaptan in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 milligrams (mg) with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Reporting group title	Tolvaptan (From 156-13-210: Placebo)

Reporting group description:

Participants were previously treated with placebo in Trial 156-13-210. Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Reporting group title	Tolvaptan (From 156-08-271: Tolvaptan)

Reporting group description:

Participants were previously treated with tolvaptan in Trial 156-08-271. Participants retained the last dose level of tolvaptan received in the trial (45/15 mg, 60/30 mg, or 90/30 mg) and started at that same dose in Trial 156-13-211.

Reporting group title	Tolvaptan (From Other: Tolvaptan)

Reporting group description:

Participants were previously treated with tolvaptan in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Reporting group title	Tolvaptan (From Other: Placebo)

Reporting group description:

Participants were previously treated with placebo in Other Trials (156-04-251 and 156-09-290). Participants initiated on tolvaptan at a split-dose of 45/15 mg with upward titration every 3 to 4 days to 60/30 mg or 90/30 mg per day according to tolerability.

Serious adverse events	Tolvaptan (From 156-13-210: Tolvaptan)	Tolvaptan (From 156-13-210: Placebo)	Tolvaptan (From 156-08-271: Tolvaptan)
Total subjects affected by serious adverse events			
subjects affected / exposed	87 / 505 (17.23%)	96 / 569 (16.87%)	103 / 717 (14.37%)
number of deaths (all causes)	1	5	3
number of deaths resulting from adverse events	1	5	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic Squamous Cell Carcinoma			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Squamous Cell Carcinoma of Head and Neck			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Squamous Cell Carcinoma			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Neoplasm			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Rectal Cancer			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Prostate Cancer			
subjects affected / exposed[1]	1 / 272 (0.37%)	1 / 280 (0.36%)	0 / 375 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary Thyroid Cancer			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian Theca Cell Tumour			
subjects affected / exposed[2]	0 / 234 (0.00%)	1 / 290 (0.34%)	0 / 343 (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
Metastases to Meninges			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Carcinoid Tumour			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Metastases to Adrenals			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Metastases to Liver			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal Cell Carcinoma			
subjects affected / exposed	2 / 505 (0.40%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Cancer Metastatic			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
B-Cell Small Lymphocytic Lymphoma			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	0 / 717 (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
Colon Cancer			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal Proliferative Breast Lesion			

subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Malignant Melanoma			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial Carcinoma			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Breast Cancer			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Vascular disorders			
Thrombophlebitis Superficial			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Shock			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Peripheral Ischaemia			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Hypotension			
subjects affected / exposed	0 / 505 (0.00%)	2 / 569 (0.35%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypertensive Crisis			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep Vein Thrombosis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteritis			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Dissection			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Aneurysm			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Hypertension			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	3 / 717 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Aneurysm			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thirst			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Oedema Peripheral			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Chest Pain			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Fatigue			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Death			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 505 (0.20%)	2 / 569 (0.35%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Chest Discomfort			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Reproductive system and breast disorders			
Rectocele			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Menorrhagia			
subjects affected / exposed[3]	1 / 234 (0.43%)	0 / 290 (0.00%)	0 / 343 (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
Breast Enlargement			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Metrorrhagia			
subjects affected / exposed[4]	0 / 234 (0.00%)	1 / 290 (0.34%)	0 / 343 (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
Respiratory, thoracic and mediastinal disorders			
Sinus Polyp			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
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 Failure			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic Pain			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Pulmonary Toxicity			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Asthma			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Epistaxis			

subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute Respiratory Failure			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute Pulmonary Oedema			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Cough			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Bronchospasm			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Panic Attack			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Suicidal Ideation			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Investigations			
Weight Decreased			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Tumour Marker Increased			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Liver Function Test Increased			
subjects affected / exposed	0 / 505 (0.00%)	3 / 569 (0.53%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International Normalised Ratio Fluctuation			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Enzyme Increased			
subjects affected / exposed	2 / 505 (0.40%)	3 / 569 (0.53%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	1 / 2	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerular Filtration Rate Decreased			

subjects affected / exposed	2 / 505 (0.40%)	3 / 569 (0.53%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases Increased			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-Reactive Protein Increased			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	2 / 505 (0.40%)	2 / 569 (0.35%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	2 / 2	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 505 (0.59%)	5 / 569 (0.88%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	3 / 3	4 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	2 / 505 (0.40%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine Aminotransferase Abnormal			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Blood Creatinine Increased			
subjects affected / exposed	1 / 505 (0.20%)	5 / 569 (0.88%)	3 / 717 (0.42%)
occurrences causally related to treatment / all	0 / 1	2 / 5	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Glucose Increased			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Urine Present			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Injury, poisoning and procedural complications			
Radius Fracture			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia Fracture			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon Rupture			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Subdural Haematoma			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Subarachnoid Haemorrhage			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Spinal Fracture			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirenal Haematoma			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic Haemothorax			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional Hernia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Humerus Fracture			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula Fracture			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	0 / 717 (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
Brain Contusion			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous Fistula Site Haematoma			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle Fracture			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic Complication			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus Injury			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental Overdose			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Polycystic Liver Disease			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urachal Abnormality			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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			
Ventricular Tachycardia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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

Pericarditis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Pericardial Effusion			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Myocardial Infarction			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral Valve Prolapse			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Left Ventricular Dysfunction			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Stenosis			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Cardiogenic Shock			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac Failure			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Arrest			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial Fibrillation			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	3 / 717 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Valve Incompetence			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Angina Unstable			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Angina Pectoris			
subjects affected / exposed	1 / 505 (0.20%)	2 / 569 (0.35%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Left Ventricular Failure			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Acute Coronary Syndrome			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 505 (0.20%)	2 / 569 (0.35%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Ruptured Cerebral Aneurysm			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Presyncope			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vith Nerve Paralysis			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Headache			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial Aneurysm			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Basilar Artery Aneurysm			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Cerebellar Ischaemia			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic Stroke			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Cerebrovascular Accident			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral Ischaemia			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Epilepsy			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 505 (0.40%)	1 / 569 (0.18%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic Anaemia			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Pancytopenia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Eye disorders			
Retinal Detachment			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Borderline Glaucoma			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diplopia			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Endocrine Ophthalmopathy			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal Disorder			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Vomiting			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Umbilical Hernia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	3 / 717 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Pancreatitis Acute			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	0 / 717 (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
Inguinal Hernia, Obstructive			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal Hernia			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated Umbilical Hernia			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Ileus			

subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	3 / 717 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis Ischaemic			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Duodenal Perforation			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Diverticulum			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 505 (0.20%)	3 / 569 (0.53%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Haematemesis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Colitis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Ascites			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain Upper			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain Lower			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain			
subjects affected / exposed	3 / 505 (0.59%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Hernia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Hepatobiliary disorders			
Bile Duct Stone			

subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Cholecystitis			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Hepatic Cyst			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Hepatic Pain			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic Hepatitis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash Vesicular			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Laxity			

subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Skin Lesion			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal Pain			
subjects affected / exposed	2 / 505 (0.40%)	5 / 569 (0.88%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Impairment			
subjects affected / exposed	6 / 505 (1.19%)	2 / 569 (0.35%)	3 / 717 (0.42%)
occurrences causally related to treatment / all	3 / 6	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Haemorrhage			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Renal Failure			
subjects affected / exposed	2 / 505 (0.40%)	1 / 569 (0.18%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cyst Haemorrhage			
subjects affected / exposed	3 / 505 (0.59%)	4 / 569 (0.70%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cyst			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Colic			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cyst Ruptured			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pollakiuria			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Nephropathy			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Kidney Injury			
subjects affected / exposed	5 / 505 (0.99%)	8 / 569 (1.41%)	7 / 717 (0.98%)
occurrences causally related to treatment / all	1 / 5	3 / 9	3 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney Enlargement			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 505 (0.20%)	2 / 569 (0.35%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End Stage Renal Disease			

subjects affected / exposed	3 / 505 (0.59%)	0 / 569 (0.00%)	8 / 717 (1.12%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Kidney Disease			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Polyuria			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Musculoskeletal and connective tissue disorders			
Spinal Osteoarthritis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Arthritis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Foot Deformity			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Arthralgia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Pain In Extremity			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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			

Pulmonary Tuberculosis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Pyelonephritis			
subjects affected / exposed	3 / 505 (0.59%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative Wound Infection			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Renal Abscess			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Renal Cyst Infection			
subjects affected / exposed	5 / 505 (0.99%)	8 / 569 (1.41%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	1 / 7	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Sepsis			
subjects affected / exposed	0 / 505 (0.00%)	2 / 569 (0.35%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	3 / 505 (0.59%)	2 / 569 (0.35%)	5 / 717 (0.70%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Infection			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Urosepsis			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	2 / 717 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia			

subjects affected / exposed	4 / 505 (0.79%)	5 / 569 (0.88%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Wall Abscess			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic Herpes Zoster			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Appendicitis Perforated			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cat Scratch Disease			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Infection			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Peritonitis Bacterial			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Diarrhoea Infectious			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Diverticulitis			
subjects affected / exposed	2 / 505 (0.40%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Bacteraemia			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Gastroenteritis			
subjects affected / exposed	2 / 505 (0.40%)	3 / 569 (0.53%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Cyst Infection			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			

subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Herpes Zoster Oticus			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected Cyst			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes Mellitus			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Hyperkalaemia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			

subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Hypoglycaemia			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (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
Hypokalaemia			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Hyponatraemia			
subjects affected / exposed	1 / 505 (0.20%)	2 / 569 (0.35%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Metabolic Acidosis			
subjects affected / exposed	0 / 505 (0.00%)	1 / 569 (0.18%)	0 / 717 (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
Obesity			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Tolvaptan (From Other: Tolvaptan)	Tolvaptan (From Other: Placebo)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	2 / 3 (66.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic Squamous Cell Carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma of Head and Neck			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Neoplasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate Cancer			
subjects affected / exposed[1]	0 / 1 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary Thyroid Cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian Theca Cell Tumour			
subjects affected / exposed[2]	0 / 5 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metastases to Meninges			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid Tumour			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to Adrenals			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to Liver			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Cell Carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Cancer Metastatic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-Cell Small Lymphocytic Lymphoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon Cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal Proliferative Breast Lesion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial Carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombophlebitis Superficial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Ischaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Crisis			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep Vein Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Dissection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Aneurysm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thirst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema Peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Discomfort			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Rectocele			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed[3]	0 / 5 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Enlargement			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed[4]	0 / 5 (0.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Sinus Polyp			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Toxicity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Pulmonary Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic Attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight Decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Marker Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Function Test Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International Normalised Ratio Fluctuation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular Filtration Rate Decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-Reactive Protein Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine Aminotransferase Abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Creatinine Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Glucose Increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Urine Present			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radius Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Fracture			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirenal Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Haemothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional Hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous Fistula Site Haematoma			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle Fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic Complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus Injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental Overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Polycystic Liver Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urachal Abnormality			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pericarditis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial Effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Infarction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral Valve Prolapse			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left Ventricular Dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Stenosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic Shock			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Valve Incompetence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Unstable			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Pectoris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Myocardial Infarction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Left Ventricular Failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Coronary Syndrome			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Ischaemic Attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ruptured Cerebral Aneurysm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vith Nerve Paralysis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial Aneurysm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar Artery Aneurysm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar Ischaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Ischaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal Detachment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Borderline Glaucoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine Ophthalmopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical Hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia, Obstructive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated Umbilical Hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis Ischaemic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile Duct Stone			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Hepatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash Vesicular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Laxity			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cyst Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Colic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cyst Ruptured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Kidney Injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney Enlargement			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
End Stage Renal Disease			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Kidney Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal Osteoarthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Deformity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain In Extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Pulmonary Tuberculosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cyst Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Wall Abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic Herpes Zoster			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis Perforated			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cat Scratch Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis Bacterial			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea Infectious			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Cyst Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster Oticus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes Mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The adverse event occurs in only male participants.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The adverse event occurs in only female participants.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The adverse event occurs in only female participants.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The adverse event occurs in only female participants.

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

Non-serious adverse events	Tolvaptan (From 156-13-210: Tolvaptan)	Tolvaptan (From 156-13-210: Placebo)	Tolvaptan (From 156-08-271: Tolvaptan)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	469 / 505 (92.87%)	525 / 569 (92.27%)	633 / 717 (88.28%)
Vascular disorders			
Hypertension			
subjects affected / exposed	87 / 505 (17.23%)	77 / 569 (13.53%)	139 / 717 (19.39%)
occurrences (all)	116	97	163
Lymphoedema			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences (all)	0	0	0
Orthostatic Hypotension			
subjects affected / exposed	1 / 505 (0.20%)	2 / 569 (0.35%)	3 / 717 (0.42%)
occurrences (all)	1	2	3
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	1 / 717 (0.14%)
occurrences (all)	1	1	1
Fatigue			
subjects affected / exposed	47 / 505 (9.31%)	74 / 569 (13.01%)	34 / 717 (4.74%)
occurrences (all)	55	85	37
Non-Cardiac Chest Pain			
subjects affected / exposed	5 / 505 (0.99%)	5 / 569 (0.88%)	4 / 717 (0.56%)
occurrences (all)	5	5	4
Oedema Peripheral			
subjects affected / exposed	32 / 505 (6.34%)	39 / 569 (6.85%)	42 / 717 (5.86%)
occurrences (all)	37	46	49
Pain			
subjects affected / exposed	6 / 505 (1.19%)	1 / 569 (0.18%)	3 / 717 (0.42%)
occurrences (all)	9	1	3
Thirst			
subjects affected / exposed	139 / 505 (27.52%)	183 / 569 (32.16%)	91 / 717 (12.69%)
occurrences (all)	176	213	99
Immune system disorders			

Type I Hypersensitivity			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal Haemorrhage			
subjects affected / exposed[5]	0 / 234 (0.00%)	1 / 290 (0.34%)	3 / 343 (0.87%)
occurrences (all)	0	1	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	27 / 505 (5.35%)	27 / 569 (4.75%)	28 / 717 (3.91%)
occurrences (all)	30	31	31
Wheezing			
subjects affected / exposed	2 / 505 (0.40%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences (all)	2	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	9 / 505 (1.78%)	9 / 569 (1.58%)	13 / 717 (1.81%)
occurrences (all)	9	9	15
Stress			
subjects affected / exposed	2 / 505 (0.40%)	4 / 569 (0.70%)	1 / 717 (0.14%)
occurrences (all)	2	4	1
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	7 / 505 (1.39%)	19 / 569 (3.34%)	17 / 717 (2.37%)
occurrences (all)	9	26	21
Blood Calcium Increased			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences (all)	0	0	1
Blood Creatinine Increased			
subjects affected / exposed	77 / 505 (15.25%)	87 / 569 (15.29%)	69 / 717 (9.62%)
occurrences (all)	104	129	87
Kidney Palpable			
subjects affected / exposed	1 / 505 (0.20%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences (all)	1	0	0
Weight Decreased			

subjects affected / exposed	4 / 505 (0.79%)	5 / 569 (0.88%)	2 / 717 (0.28%)
occurrences (all)	4	6	3
Weight Increased			
subjects affected / exposed	1 / 505 (0.20%)	3 / 569 (0.53%)	4 / 717 (0.56%)
occurrences (all)	1	3	5
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 505 (1.58%)	9 / 569 (1.58%)	11 / 717 (1.53%)
occurrences (all)	10	10	11
Cardiac disorders			
Left Ventricular Hypertrophy			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	5 / 505 (0.99%)	6 / 569 (1.05%)	14 / 717 (1.95%)
occurrences (all)	5	6	15
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 505 (3.56%)	31 / 569 (5.45%)	31 / 717 (4.32%)
occurrences (all)	20	37	37
Headache			
subjects affected / exposed	51 / 505 (10.10%)	72 / 569 (12.65%)	51 / 717 (7.11%)
occurrences (all)	61	83	68
Tremor			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	2 / 717 (0.28%)
occurrences (all)	1	1	2
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	3 / 505 (0.59%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences (all)	3	0	1
Motion Sickness			
subjects affected / exposed	1 / 505 (0.20%)	1 / 569 (0.18%)	0 / 717 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Abdominal Discomfort			

subjects affected / exposed	9 / 505 (1.78%)	14 / 569 (2.46%)	4 / 717 (0.56%)
occurrences (all)	10	16	5
Abdominal Hernia			
subjects affected / exposed	7 / 505 (1.39%)	1 / 569 (0.18%)	6 / 717 (0.84%)
occurrences (all)	7	1	6
Abdominal Pain Lower			
subjects affected / exposed	6 / 505 (1.19%)	6 / 569 (1.05%)	6 / 717 (0.84%)
occurrences (all)	6	7	6
Abdominal Pain Upper			
subjects affected / exposed	20 / 505 (3.96%)	19 / 569 (3.34%)	12 / 717 (1.67%)
occurrences (all)	24	24	12
Constipation			
subjects affected / exposed	16 / 505 (3.17%)	28 / 569 (4.92%)	10 / 717 (1.39%)
occurrences (all)	17	34	11
Diarrhoea			
subjects affected / exposed	37 / 505 (7.33%)	38 / 569 (6.68%)	33 / 717 (4.60%)
occurrences (all)	41	43	39
Dry Mouth			
subjects affected / exposed	22 / 505 (4.36%)	38 / 569 (6.68%)	3 / 717 (0.42%)
occurrences (all)	24	41	4
Dyspepsia			
subjects affected / exposed	17 / 505 (3.37%)	27 / 569 (4.75%)	10 / 717 (1.39%)
occurrences (all)	19	28	10
Gastrooesophageal Reflux Disease			
subjects affected / exposed	11 / 505 (2.18%)	19 / 569 (3.34%)	17 / 717 (2.37%)
occurrences (all)	11	22	17
Gingival Pain			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	1 / 717 (0.14%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	37 / 505 (7.33%)	51 / 569 (8.96%)	38 / 717 (5.30%)
occurrences (all)	40	59	40
Vomiting			
subjects affected / exposed	24 / 505 (4.75%)	38 / 569 (6.68%)	32 / 717 (4.46%)
occurrences (all)	27	41	36
Skin and subcutaneous tissue disorders			

Dermatitis Contact			
subjects affected / exposed	7 / 505 (1.39%)	4 / 569 (0.70%)	3 / 717 (0.42%)
occurrences (all)	9	5	3
Renal and urinary disorders			
Chronic Kidney Disease			
subjects affected / exposed	4 / 505 (0.79%)	6 / 569 (1.05%)	7 / 717 (0.98%)
occurrences (all)	4	6	7
Haematuria			
subjects affected / exposed	27 / 505 (5.35%)	52 / 569 (9.14%)	48 / 717 (6.69%)
occurrences (all)	34	63	53
Nocturia			
subjects affected / exposed	77 / 505 (15.25%)	124 / 569 (21.79%)	58 / 717 (8.09%)
occurrences (all)	105	150	63
Pollakiuria			
subjects affected / exposed	27 / 505 (5.35%)	34 / 569 (5.98%)	12 / 717 (1.67%)
occurrences (all)	36	38	18
Polyuria			
subjects affected / exposed	117 / 505 (23.17%)	180 / 569 (31.63%)	53 / 717 (7.39%)
occurrences (all)	141	203	56
Renal Cyst Ruptured			
subjects affected / exposed	4 / 505 (0.79%)	9 / 569 (1.58%)	7 / 717 (0.98%)
occurrences (all)	4	12	8
Renal Impairment			
subjects affected / exposed	12 / 505 (2.38%)	29 / 569 (5.10%)	14 / 717 (1.95%)
occurrences (all)	12	31	16
Renal Pain			
subjects affected / exposed	98 / 505 (19.41%)	110 / 569 (19.33%)	141 / 717 (19.67%)
occurrences (all)	139	179	209
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	33 / 505 (6.53%)	25 / 569 (4.39%)	26 / 717 (3.63%)
occurrences (all)	42	26	36
Back Pain			
subjects affected / exposed	53 / 505 (10.50%)	57 / 569 (10.02%)	51 / 717 (7.11%)
occurrences (all)	59	71	55
Infections and infestations			

Bronchitis			
subjects affected / exposed	23 / 505 (4.55%)	29 / 569 (5.10%)	31 / 717 (4.32%)
occurrences (all)	25	34	35
Ear Infection			
subjects affected / exposed	8 / 505 (1.58%)	9 / 569 (1.58%)	5 / 717 (0.70%)
occurrences (all)	9	9	8
Gastroenteritis			
subjects affected / exposed	14 / 505 (2.77%)	22 / 569 (3.87%)	41 / 717 (5.72%)
occurrences (all)	15	24	44
Gingivitis			
subjects affected / exposed	2 / 505 (0.40%)	3 / 569 (0.53%)	2 / 717 (0.28%)
occurrences (all)	2	3	2
Influenza			
subjects affected / exposed	34 / 505 (6.73%)	43 / 569 (7.56%)	39 / 717 (5.44%)
occurrences (all)	38	49	52
Nasopharyngitis			
subjects affected / exposed	92 / 505 (18.22%)	100 / 569 (17.57%)	94 / 717 (13.11%)
occurrences (all)	129	143	123
Sinusitis			
subjects affected / exposed	22 / 505 (4.36%)	31 / 569 (5.45%)	35 / 717 (4.88%)
occurrences (all)	30	37	47
Upper Respiratory Tract Infection			
subjects affected / exposed	58 / 505 (11.49%)	53 / 569 (9.31%)	86 / 717 (11.99%)
occurrences (all)	64	83	129
Urinary Tract Infection			
subjects affected / exposed	52 / 505 (10.30%)	58 / 569 (10.19%)	65 / 717 (9.07%)
occurrences (all)	86	79	117
Vulvovaginal Mycotic Infection			
subjects affected / exposed[6]	3 / 234 (1.28%)	1 / 290 (0.34%)	6 / 343 (1.75%)
occurrences (all)	3	1	7
Zika Virus Infection			
subjects affected / exposed	0 / 505 (0.00%)	0 / 569 (0.00%)	0 / 717 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased Appetite			

subjects affected / exposed	8 / 505 (1.58%)	18 / 569 (3.16%)	4 / 717 (0.56%)
occurrences (all)	9	19	4
Gout			
subjects affected / exposed	28 / 505 (5.54%)	25 / 569 (4.39%)	30 / 717 (4.18%)
occurrences (all)	49	46	42
Hyperlipidaemia			
subjects affected / exposed	4 / 505 (0.79%)	5 / 569 (0.88%)	7 / 717 (0.98%)
occurrences (all)	5	5	7
Polydipsia			
subjects affected / exposed	27 / 505 (5.35%)	53 / 569 (9.31%)	14 / 717 (1.95%)
occurrences (all)	29	54	14

Non-serious adverse events	Tolvaptan (From Other: Tolvaptan)	Tolvaptan (From Other: Placebo)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	
occurrences (all)	4	1	
Lymphoedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Orthostatic Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Oedema Peripheral			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Thirst			
subjects affected / exposed	4 / 6 (66.67%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Immune system disorders			
Type I Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vaginal Haemorrhage			
subjects affected / exposed[5]	0 / 5 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood Calcium Increased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood Creatinine Increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Kidney Palpable			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Weight Decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Weight Increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Left Ventricular Hypertrophy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Tremor			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			

Hypoacusis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Motion Sickness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Abdominal Hernia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Abdominal Pain Lower			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Abdominal Pain Upper			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Dry Mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Gingival Pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis Contact			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Chronic Kidney Disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	2	
Nocturia			
subjects affected / exposed	3 / 6 (50.00%)	1 / 3 (33.33%)	
occurrences (all)	4	2	
Pollakiuria			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Polyuria			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Renal Cyst Ruptured			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Renal Impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Renal Pain			

subjects affected / exposed	3 / 6 (50.00%)	2 / 3 (66.67%)	
occurrences (all)	4	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Back Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Ear Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Urinary Tract Infection			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal Mycotic Infection			
subjects affected / exposed[6]	0 / 5 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Zika Virus Infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Hyperlipidaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Polydipsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Notes:

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The adverse event occurs in only female participants.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The adverse event occurs in only female participants.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2014	Protocol procedures were revised to accommodate the treatment and monitoring of participants enrolling into the protocol from additional tolvaptan trials. The sample size was increased, the inclusion criteria were slightly modified, schedules for initiation of treatment and liver function testing were further defined, and pharmacokinetic sampling was included to assess compliance.
06 March 2015	The window was increased from 30 days to up to 3 months to allow use of historical laboratory values for screening, to add flexibility and allow combining of screening and baseline visits in the trial, and to provide clarification on trial discontinuation.

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.

None

Notes: