Clinical trial results:
A Randomized, Placebo Controlled, Parallel-Group, Double Blind Efficacy and Safety Trial of MK-8931 with a Long Term Double-Blind Extension in Subjects with Mild to Moderate Alzheimer's Disease (Protocol No. MK-8931-017-10)(also known as SCH 900931, P07738)

Summary

EudraCT number	2011-003151-20
Trial protocol	ES NL GB IT DE PT HU BE AT DK
Global end of trial date	14 April 2017

Results information

Result version number	v1 (current)
This version publication date	27 April 2018
First version publication date	27 April 2018

Trial information

Trial identification

Sponsor protocol code	8931-017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01739348
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-8931-017

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	14 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study includes a Part I and Part II. Part I assesses efficacy and safety of verubecestat (MK-8931) compared with placebo administered for 78 weeks for treatment of Alzheimer's Disease (AD). The primary hypotheses for Part I are that ≥1 verubecestat dose is superior to placebo at 78 weeks of treatment with respect to change from baseline in: 1) AD Assessment Scale Cognitive Subscale (ADAS-Cog) score; and 2) AD Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) score. Participants completing Part I may continue to Part II, a double-blind extension to assess efficacy and safety of verubecestat given for an additional 260 weeks. Part I includes 2 substudies conducted at select sites: 1) a positron emission tomography (PET) imaging substudy evaluating changes in brain amyloid protein load using an amyloid tracer ([18F]flutemetamol); and 2) a cerebrospinal fluid (CSF) biomarker substudy to evaluate changes in amyloid-β related peptides, total tau, and phosphorylated tau.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Austria: 19
Country: Number of subjects enrolled	Belgium: 51
Country: Number of subjects enrolled	Brazil: 43
Country: Number of subjects enrolled	Canada: 84
Country: Number of subjects enrolled	Denmark: 54
Country: Number of subjects enrolled	Argentina: 91
Country: Number of subjects enrolled	France: 128
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Hungary: 35
Country: Number of subjects enrolled	Israel: 25
Country: Number of subjects enrolled	Italy: 27
Country: Number of subjects enrolled	Japan: 295
Country: Number of subjects enrolled	Korea, Republic of: 54

Country: Number of subjects enrolled	Netherlands: 43
Country: Number of subjects enrolled	New Zealand: 20
Country: Number of subjects enrolled	Portugal: 57
Country: Number of subjects enrolled	Spain: 102
Country: Number of subjects enrolled	Turkey: 56
Country: Number of subjects enrolled	United Kingdom: 71
Country: Number of subjects enrolled	United States: 885
Worldwide total number of subjects	2211
EEA total number of subjects	623

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)	398
From 65 to 84 years	1771
85 years and over	42

Subject disposition

Recruitment

Recruitment details:

Part I began by enrolling approximately 50 participants per arm (200 total). Enrollment continued until the first 200 participants reached 13 weeks treatment; total enrollment at that time: ~400. For these ~400 participants (Safety Cohort), an interim analysis (IA) was conducted to assess safety. Following IA, enrollment continued (Main Cohort).

Pre-assignment

Screening details:

2211 participants were randomized in Part I, with 2210 receiving treatment. As planned per protocol, no participants were randomized to the Verubecestat 60 mg arm (Arm C) in the Main Cohort. Participants completing Part I were eligible to continue to Part II. The trial was terminated early and did not complete as planned.

Period 1

Period 1 title	Part I (Base Study)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]

Arm description:

[Part I] Verubecestat 12 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 12 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931, MK-8931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Arm title	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]

Arm description:

[Part I] Verubecestat 40 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931, MK-8931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Arm title	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]

Arm description:

[Part I] Verubecestat 60 mg once daily until the first IA in Study Part I (Base Study). Following IA,

participants in this group were switched to Verubecestat 40 mg once daily, for the remainder of Study Part I (total dosing period: 78 weeks). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931, MK-8931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Arm title	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]

Arm description:

[Part I] Placebo once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

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

Dosage and administration details:

Single placebo tablet matching verubecestat treatment once daily, taken orally

Number of subjects in period 1	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]
Started	703	700	103
Treated	702	700	103
Completed	501	497	77
Not completed	202	203	26
Adverse event, serious fatal	10	7	2
Physician decision	10	7	1
Screen Failure	2	-	-
Site Discontinued Study Participation	1	3	-
Participant Moved	4	3	1
Study Terminated by Sponsor	72	73	-
Consent withdrawn by subject	23	21	7
Non-Compliance with Study Drug	3	2	-
Adverse event, non-fatal	41	52	8
Trial Partner/Caregiver Withdrew Consent	27	25	2
Lost to follow-up	4	2	4
Lack of efficacy	3	8	-
Protocol deviation	2	-	1

Number of subjects in period 1	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Started	705
Treated	705
Completed	516
Not completed	189
Adverse event, serious fatal	8
Physician decision	4
Screen Failure	-
Site Discontinued Study Participation	-
Participant Moved	7
Study Terminated by Sponsor	86
Consent withdrawn by subject	20
Non-Compliance with Study Drug	-
Adverse event, non-fatal	33
Trial Partner/Caregiver Withdrew Consent	18
Lost to follow-up	4
Lack of efficacy	7
Protocol deviation	2

Period 2

Period 2 title	Part II (Extension Study)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]

Arm description:

[Part I] Verubecestat 12 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 12 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931, MK-8931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Arm title	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]

Arm description:

[Part I] Verubecestat 40 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931, MK-8931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Arm title	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]

Arm description:

[Part I] Verubecestat 60 mg once daily until the first IA in Study Part I (Base Study). Following IA, participants in this group were switched to Verubecestat 40 mg once daily, for the remainder of Study Part I (total dosing period: 78 weeks). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931, MK-8931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Arm title	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]

Arm description:

[Part I] Placebo once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Arm type	Experimental
Investigational medicinal product name	Verubecestat
Investigational medicinal product code	
Other name	SCH 900931
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single verubecestat tablet (12 mg, 40 mg or 60 mg) once daily, taken orally

Number of subjects in period 2[1]	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]
Started	379	366	61
Treated	379	365	61
Completed	0	0	0
Not completed	379	366	61
Adverse event, serious fatal	3	3	2
Physician decision	7	11	6
Consent withdrawn by subject	5	2	4
Non-Compliance with Study Drug	-	-	-
Adverse event, non-fatal	10	11	7
Trial Partner/Caregiver Withdrew Consent	18	12	8
Participant Moved	3	3	-
Study Terminated by Sponsor	329	315	34
Lost to follow-up	3	4	-
Lack of efficacy	1	5	-

Number of subjects in period 2[1]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Started	396
Treated	394
Completed	0
Not completed	396
Adverse event, serious fatal	6
Physician decision	12
Consent withdrawn by subject	7
Non-Compliance with Study Drug	1
Adverse event, non-fatal	26
Trial Partner/Caregiver Withdrew Consent	16
Participant Moved	3
Study Terminated by Sponsor	323
Lost to follow-up	1
Lack of efficacy	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Number started refers to participants completing Part I, continuing to Part II

Baseline characteristics

Reporting groups	
Reporting group title	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 12 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 12 mg once daily for an additional 260 weeks.	
Reporting group title	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 40 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 60 mg once daily until the first IA in Study Part I (Base Study). Following IA, participants in this group were switched to Verubecestat 40 mg once daily, for the remainder of Study Part I (total dosing period: 78 weeks). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Reporting group description:	
[Part I] Placebo once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	

Reporting group values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]
Number of subjects	703	700	103
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	131	130	17
From 65-84 years	561	556	82
85 years and over	11	14	4
Age Continuous Units: Years			
arithmetic mean	71.2	71.8	72.3
standard deviation	± 7.4	± 7.6	± 7.4
Sex: Female, Male Units: Subjects			
Female	383	403	56
Male	320	297	47
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	3	0

Asian	118	125	11
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	8	13	2
White	566	547	88
More than one race	4	4	2
Unknown or Not Reported	6	8	0
Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) Score			
ADAS-Cog measures cognition by assessing 11 metrics impaired in Alzheimer's Disease (AD). For each metric, scores range from 0 (no impairment) to (depending on metric) either 5 (8 metrics), 8, 10, or 12 (1 metric each); higher scores indicate more severe impairment. Individual scores sum to a total ADAS-Cog score (range: 0-70). Higher total scores indicate greater cognitive impairment. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose ADAS-Cog observation (Full Analysis Set [FAS] population). For Arms A, B, C, and D, N= 681, 672, 97, and 694.			
Units: Score on a Scale			
arithmetic mean	21.4	21.3	20.6
standard deviation	± 7.5	± 7.6	± 6.2
Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) Score			
ADCS-ADL measures performance of activities of daily living, calculated from a 24-question survey; question scores range from 0 (no independence) to either 2 (1 question), 3 (17 questions), 4 (5 questions), or 5 (1 question). Higher scores indicate greater independence in performance. Scores from questions sum to a total ADCS-ADL score (range: 0-78). Lower scores indicate less independence in performance. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose ADCS-ADL observation (FAS population). For Arms A, B, C, and D, N= 677, 668, 98, and 686.			
Units: Score on a Scale			
arithmetic mean	63.0	62.9	63.5
standard deviation	± 9.5	± 9.8	± 10.3
Clinical Dementia Rating Sum of Boxes (CDR-SB) Score			
CDR-SB is a clinical rating of global cognitive function, comprised of 6 domains. For each domain, degree of impairment is assessed by semi-structured interview of the participant and the participant's caregiver. For each domain, potential scores range from 0 (no impairment) to 3 (severe impairment). Domain scores sum to a total CDR-SB score (range: 0-18). Higher scores indicate more severe cognitive impairment. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose CDR-SB observation (FAS population). For Arms A, B, C, and D, N= 660, 643, 91, and 673.			
Units: Score on a Scale			
arithmetic mean	5.4	5.3	5.5
standard deviation	± 2.1	± 2.1	± 2.3
Total Hippocampal Volume			
Total Hippocampal Volume (THV) was measured by volumetric magnetic resonance imaging (vMRI). Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose observation for THV (FAS population). For Arms A, B, C, and D, N= 332, 307, 55, and 346.			
Units: Microliters			
arithmetic mean	5894.1	5823.4	5653.5
standard deviation	± 1231.5	± 1189.9	± 1148.4
Cerebrospinal Fluid (CSF) Total Tau Concentration			
Total Tau concentration in the cerebrospinal fluid (CSF) was monitored as a measure of brain tau pathology. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose observation for CSF Total Tau (FAS population). Per protocol, CSF Total Tau concentration was analyzed as part of a substudy in Part I, with testing occurring at select trial sites. For Arms A, B, C, and D, N= 38, 57, 12, and 41.			
Units: picograms (pg)/mL			
arithmetic mean	206.7	231.5	268.6
standard deviation	± 90.4	± 113.9	± 136.2
[18F]Flutemetamol Positron Emission Tomography (PET) Standard Uptake			

Value Ratio (SUVR)			
Brain amyloid load assessed by SUVR of intravenous (IV) [18F]Flutemetamol. After administration and PET scan, regions of interest (ROIs) are assessed for regional SUVR, defined as ratio of pixel intensity at ROI compared to reference region (RR). Regional SUVRs are averaged for composite SUVR; higher values indicate increased amyloid load. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose SUVR observation (FAS population). Excludes participants enrolled before IA and to Arm C. For Arms A, B, C, and D, N= 20, 10, 0, and 14. '9999': no data collected.			
Units: SUVR			
arithmetic mean	0.89	0.87	9999
standard deviation	± 0.10	± 0.11	± 9999
Neuropsychiatric Inventory (NPI) Score			
NPI assesses psychiatric status in 12 domains. After interview of participant's caregiver, domains scored on symptom frequency [range: 1 (occasional) to 4 (very frequent)] and severity [range: 1 (mild) to 3 (severe)]. Domain scores (range: 0-12) are product of frequency and severity scores; if no symptoms, score is 0. Domain scores sum to total NPI score (range: 0-144). Higher scores reflect more severe impairment. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose NPI observation (FAS population). For Arms A, B, C, and D, N= 682, 679, 100, and 691.			
Units: Score on a Scale			
arithmetic mean	8.7	8.2	6.9
standard deviation	± 10.5	± 9.8	± 9.5
Mini-Mental State Examination (MMSE) Score			
MMSE is a cognitive assessment of 5 domains with 11 total questions related to the participant, scored based on the number of correct responses; depending on question, potential scores range from 0 (no correct response) to either 1 (4 questions), 2 (1 question), 3 (3 questions), or 5 (3 questions). Scores from each question sum to a total MMSE score (range: 0-30); higher scores indicate better cognitive performance. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose MMSE observation (FAS population). For Arms A, B, C, and D, N= 660, 648, 98, and 679.			
Units: Score on a Scale			
arithmetic mean	20.4	20.2	20.6
standard deviation	± 3.3	± 3.3	± 3.3

Reporting group values	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]	Total	
Number of subjects	705	2211	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	120	398	
From 65-84 years	572	1771	
85 years and over	13	42	
Age Continuous			
Units: Years			
arithmetic mean	72.4		
standard deviation	± 7.6	-	
Sex: Female, Male			
Units: Subjects			
Female	376	1218	
Male	329	993	

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	7	
Asian	115	369	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	7	30	
White	578	1779	
More than one race	0	10	
Unknown or Not Reported	2	16	
Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) Score			
ADAS-Cog measures cognition by assessing 11 metrics impaired in Alzheimer's Disease (AD). For each metric, scores range from 0 (no impairment) to (depending on metric) either 5 (8 metrics), 8, 10, or 12 (1 metric each); higher scores indicate more severe impairment. Individual scores sum to a total ADAS-Cog score (range: 0-70). Higher total scores indicate greater cognitive impairment. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose ADAS-Cog observation (Full Analysis Set [FAS] population). For Arms A, B, C, and D, N= 681, 672, 97, and 694.			
Units: Score on a Scale			
arithmetic mean	21.7		
standard deviation	± 7.6	-	
Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) Score			
ADCS-ADL measures performance of activities of daily living, calculated from a 24-question survey; question scores range from 0 (no independence) to either 2 (1 question), 3 (17 questions), 4 (5 questions), or 5 (1 question). Higher scores indicate greater independence in performance. Scores from questions sum to a total ADCS-ADL score (range: 0-78). Lower scores indicate less independence in performance. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose ADCS-ADL observation (FAS population). For Arms A, B, C, and D, N= 677, 668, 98, and 686.			
Units: Score on a Scale			
arithmetic mean	62.1		
standard deviation	± 10.4	-	
Clinical Dementia Rating Sum of Boxes (CDR-SB) Score			
CDR-SB is a clinical rating of global cognitive function, comprised of 6 domains. For each domain, degree of impairment is assessed by semi-structured interview of the participant and the participant's caregiver. For each domain, potential scores range from 0 (no impairment) to 3 (severe impairment). Domain scores sum to a total CDR-SB score (range: 0-18). Higher scores indicate more severe cognitive impairment. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose CDR-SB observation (FAS population). For Arms A, B, C, and D, N= 660, 643, 91, and 673.			
Units: Score on a Scale			
arithmetic mean	5.6		
standard deviation	± 2.3	-	
Total Hippocampal Volume			
Total Hippocampal Volume (THV) was measured by volumetric magnetic resonance imaging (vMRI). Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose observation for THV (FAS population). For Arms A, B, C, and D, N= 332, 307, 55, and 346.			
Units: Microliters			
arithmetic mean	5800.7		
standard deviation	± 1069.2	-	
Cerebrospinal Fluid (CSF) Total Tau Concentration			
Total Tau concentration in the cerebrospinal fluid (CSF) was monitored as a measure of brain tau pathology. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose observation for CSF Total Tau (FAS population). Per protocol, CSF Total Tau concentration was analyzed as part of a substudy in Part I, with testing occurring at select trial sites. For Arms A, B, C, and D, N= 38, 57, 12, and 41.			
Units: picograms (pg)/mL			

arithmetic mean	246.2		
standard deviation	± 192.9	-	
[18F]Flutemetamol Positron Emission Tomography (PET) Standard Uptake Value Ratio (SUVR)			
Brain amyloid load assessed by SUVR of intravenous (IV) [18F]Flutemetamol. After administration and PET scan, regions of interest (ROIs) are assessed for regional SUVR, defined as ratio of pixel intensity at ROI compared to reference region (RR). Regional SUVRs are averaged for composite SUVR; higher values indicate increased amyloid load. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose SUVR observation (FAS population). Excludes participants enrolled before IA and to Arm C. For Arms A, B, C, and D, N= 20, 10, 0, and 14. '9999': no data collected.			
Units: SUVR			
arithmetic mean	0.88		
standard deviation	± 0.11	-	
Neuropsychiatric Inventory (NPI) Score			
NPI assesses psychiatric status in 12 domains. After interview of participant's caregiver, domains scored on symptom frequency [range: 1 (occasional) to 4 (very frequent)] and severity [range: 1 (mild) to 3 (severe)]. Domain scores (range: 0-12) are product of frequency and severity scores; if no symptoms, score is 0. Domain scores sum to total NPI score (range: 0-144). Higher scores reflect more severe impairment. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose NPI observation (FAS population). For Arms A, B, C, and D, N= 682, 679, 100, and 691.			
Units: Score on a Scale			
arithmetic mean	9.2		
standard deviation	± 11.6	-	
Mini-Mental State Examination (MMSE) Score			
MMSE is a cognitive assessment of 5 domains with 11 total questions related to the participant, scored based on the number of correct responses; depending on question, potential scores range from 0 (no correct response) to either 1 (4 questions), 2 (1 question), 3 (3 questions), or 5 (3 questions). Scores from each question sum to a total MMSE score (range: 0-30); higher scores indicate better cognitive performance. Includes all randomized participants with a baseline and ≥1 within-analysis-window, post-dose MMSE observation (FAS population). For Arms A, B, C, and D, N= 660, 648, 98, and 679.			
Units: Score on a Scale			
arithmetic mean	20.3		
standard deviation	± 3.2	-	

End points

End points reporting groups

Reporting group title	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 12 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 12 mg once daily for an additional 260 weeks.	
Reporting group title	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 40 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 60 mg once daily until the first IA in Study Part I (Base Study). Following IA, participants in this group were switched to Verubecestat 40 mg once daily, for the remainder of Study Part I (total dosing period: 78 weeks). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Reporting group description:	
[Part I] Placebo once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 12 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 12 mg once daily for an additional 260 weeks.	
Reporting group title	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 40 mg once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]
Reporting group description:	
[Part I] Verubecestat 60 mg once daily until the first IA in Study Part I (Base Study). Following IA, participants in this group were switched to Verubecestat 40 mg once daily, for the remainder of Study Part I (total dosing period: 78 weeks). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	
Reporting group title	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Reporting group description:	
[Part I] Placebo once daily for 78 weeks in Study Part I (Base Study). [Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.	

Primary: [Part I (Base Study)] Change from Baseline in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) Score

End point title	[Part I (Base Study)] Change from Baseline in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) Score
End point description:	
Least squares mean change from baseline (CFB) at week 78 was assessed for ADAS-Cog score. ADAS-Cog measures cognition by 11 metrics impaired in AD: speech; speech comprehension; word finding; word recall; object/finger naming; orientation; obeying commands; ideational praxis; constructional	

praxis; word recognition; and remembering instruction. For each metric, scores range from 0 (no impairment) to (depending on metric) either 5 (8 metrics), 8, 10, or 12 (1 metric each); higher scores indicate more severe impairment. Individual scores sum to a total ADAS-Cog score (range: 0-70); higher total scores indicate greater cognitive impairment and AD severity. Further, increases in AD severity are reflected by increases in ADAS-Cog score. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose ADAS-Cog observation (FAS population).

End point type	Primary
End point timeframe:	
Baseline and week 78	

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	631[1]	626[2]	0[3]	644[4]
Units: Score on a Scale				
least squares mean (confidence interval 95%)	7.9 (7.2 to 8.6)	8.0 (7.3 to 8.7)	(to)	7.7 (7.0 to 8.4)

Notes:

[1] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[2] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[3] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[4] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	ADAS-Cog CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II] v Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]
Number of subjects included in analysis	1275
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6287
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	0.2
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-0.9
upper limit	1.3

Statistical analysis title	ADAS-Cog CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]

Number of subjects included in analysis	1270
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4625
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	0.4
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-0.8
upper limit	1.5

Primary: [Part I (Base Study)] Change from Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) Score

End point title	[Part I (Base Study)] Change from Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) Score

End point description:

Least squares mean CFB at week 78 was assessed for ADCS-ADL score. ADCS-ADL measures performance of activities of daily living, calculated from a 24-question survey. For each of the 24 questions, scores range from 0 (no independence) to (depending on the question) either 2 (1 question), 3 (17 questions), 4 (5 questions), or 5 (1 question); higher scores indicate greater independence in activity performance. Scores from individual questions sum to a total ADCS-ADL score (range: 0 to 78); lower scores indicate less independence in activity performance and, as a result, greater AD severity. Further, increases in AD severity over time would be reflected by decreases in ADCS-ADL score. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose ADCS-ADL observation (FAS population).

End point type	Primary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	627[5]	622[6]	0[7]	636[8]
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-8.4 (-9.5 to -7.4)	-8.2 (-9.2 to -7.1)	(to)	-8.9 (-9.9 to -8.0)

Notes:

[5] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[6] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[7] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[8] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	ADAS-ADL CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4925
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.5
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-1.1
upper limit	2.1

Statistical analysis title	ADAS-Cog CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1258
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3221
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.7
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-0.9
upper limit	2.3

Primary: [Part II (Extension Study)] Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) Score

End point title	[Part II (Extension Study)] Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) Score[9]

End point description:

Mean CFB at week 104 was assessed for ADAS-Cog score. ADAS-Cog measures cognition by 11 metrics impaired in AD: speech; speech comprehension; word finding; word recall; object/finger naming; orientation; obeying commands; ideational praxis; constructional praxis; word recognition; and remembering instruction. For each metric, scores range from 0 (no impairment) to (depending on metric) either 5 (8 metrics), 8, 10, or 12 (1 metric each); higher scores indicate more severe impairment. Individual scores sum to a total ADAS-Cog score (range: 0-70); higher scores indicate greater cognitive impairment and AD severity. Further, increases in AD severity are reflected by increases in ADAS-Cog score. Analysis population: all randomized participants continuing to Part II, with a baseline (from Part I) and ≥1 within-analysis-window, post-dose ADAS-Cog observation (FAS population), having an ADAS-Cog observation at week 104.

End point type	Primary

End point timeframe:

Baseline and week 104

Notes:

[9] - 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: Given the negative results for the coprimary endpoints (base study), the analyses in the extension were not conducted.

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	207[10]	208[11]	0[12]	216[13]
Units: Score on a Scale				
arithmetic mean (standard deviation)	10.1 (± 9.9)	8.5 (± 9.5)	()	9.6 (± 9.5)

Notes:

[10] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[11] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[12] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[13] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

No statistical analyses for this end point

Primary: [Part II (Extension Study)] Change from Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) Score

End point title	[Part II (Extension Study)] Change from Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) Score[14]

End point description:

Mean CFB at week 104 was assessed for the ADCS-ADL score. The ADCS-ADL score measures the performance of activities of daily living, calculated from a 24-question survey. For each of the 24 questions, scores range from 0 (no independence) to (depending on the question) either 2 (1 question), 3 (17 questions), 4 (5 questions), or 5 (1 question), with higher scores indicating greater independence in activity performance. Scores from individual questions are summed into a total ADCS-ADL score, with total scores ranging from 0 to 78. Lower scores indicate less independence in activity performance and, as a result, greater AD severity. Further, increases in AD severity over time would be reflected by decreases in ADCS-ADL score. Analysis population: all randomized participants continuing to Part II, with a baseline (from Part I) and ≥1 within-analysis-window, post-dose ADAS-Cog observation (FAS population), having an ADAS-Cog observation at week 104.

End point type	Primary

End point timeframe:

Baseline and week 104

Notes:

[14] - 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: Given the negative results for the coprimary endpoints (base study), the analyses in the extension were not conducted.

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	207[15]	209[16]	0[17]	216[18]
Units: Score on a Scale				
arithmetic mean (standard deviation)	-10.7 (± 13.7)	-9.2 (± 12.7)	()	-9.3 (± 12.0)

Notes:

[15] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[16] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[17] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[18] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

No statistical analyses for this end point

Primary: [Part I (Base Study)] Number of Participants Who Experienced an Adverse Event

End point title	[Part I (Base Study)] Number of Participants Who Experienced an Adverse Event[19]

End point description:

The number of participants experiencing an adverse event (AE) in Part I was assessed. An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor’s product is also an AE. Analysis population: all randomized participants in Part I receiving ≥1 dose of trial treatment.

End point type	Primary

End point timeframe:

Up to week 80 (up to 2 weeks following cessation of study treatment in Part I)

Notes:

[19] - 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: Per protocol, primary statistical analyses were not planned for this endpoint.

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	702	700	103	705
Units: Participants	630	646	90	579

Statistical analyses

No statistical analyses for this end point

Primary: [Part II (Extension Study)] Number of Participants Who Experienced an Adverse Event

End point title	[Part II (Extension Study)] Number of Participants Who Experienced an Adverse Event[20]

End point description:

The number of participants experiencing an adverse event (AE) in Part II was assessed. An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product is also an AE. Analysis population: all randomized participants continuing to Part II, receiving ≥1 dose of trial treatment in Part II. For included participants, the data reflect AEs occurring in Part II only.

End point type	Primary

End point timeframe:

From week 78 (end of treatment in Part I) up to week 262 of Part II

Notes:

[20] - 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: Per protocol, primary statistical analyses were not planned for this endpoint.

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	379	365	61	394
Units: Participants	240	230	51	264

Statistical analyses

No statistical analyses for this end point

Primary: [Part I (Base Study)] Number of Participants who Discontinued from Study Drug due to an Adverse Event

End point title	[Part I (Base Study)] Number of Participants who Discontinued from Study Drug due to an Adverse Event[21]

End point description:

The number of participants discontinuing from study drug due to an AE in Part I was assessed. An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product is also an AE. Analysis population: all randomized participants in Part I receiving ≥1 dose of trial treatment.

End point type	Primary

End point timeframe:

Up to week 78

Notes:

[21] - 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: Per protocol, primary statistical analyses were not planned for this endpoint.

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	702	700	103	705
Units: Participants	57	64	12	42

Statistical analyses

No statistical analyses for this end point

Primary: [Part II (Extension Study)] Number of Participants who Discontinued from Study Drug due to an Adverse Event

End point title	[Part II (Extension Study)] Number of Participants who Discontinued from Study Drug due to an Adverse Event[22]

End point description:

The number of participants discontinuing from study drug due to an AE in Part II was assessed. An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product is also an AE. Analysis population: all randomized participants continuing to Part II, receiving ≥1 dose of trial treatment in Part II. For included participants, the data reflect treatment discontinuations occurring in Part II only.

End point type	Primary

End point timeframe:

From week 78 (end of treatment in Part I) up to week 260 of Part II

Notes:

[22] - 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: Per protocol, primary statistical analyses were not planned for this endpoint.

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	379	365	61	394
Units: Participants	10	9	6	29

Statistical analyses

No statistical analyses for this end point

Secondary: [Part I (Base Study)] Change from Baseline in Clinical Dementia Rating Sum of Boxes (CDR-SB) Score

End point title	[Part I (Base Study)] Change from Baseline in Clinical Dementia Rating Sum of Boxes (CDR-SB) Score

End point description:

Least squares mean CFB at week 78 was assessed for CDR-SB score. CDR-SB score is a clinical rating of global cognitive function, comprised of 6 domains including: memory; orientation; judgment and problem solving; community affairs; home and hobbies; and personal care. For each domain, the degree of impairment is assessed by a semi-structured interview of the participant as well as the participant's caregiver. For each domain, potential scores range from 0 (no impairment) to 3 (severe impairment). Scores from each individual domain are summed to the total CDR-SB score, with total scores ranging from 0-18. Higher scores indicate more severe cognitive impairment. Further, increases in cognitive impairment would be reflected by increases in CDR-SB score. Analysis population: all randomized participants (Part I) with a baseline and ≥1 within-analysis-window, post-dose observation for CDR-SB (FAS population).

End point type	Secondary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	611[23]	600[24]	0[25]	623[26]
Units: Score on a Scale				
least squares mean (confidence interval 95%)	2.1 (1.8 to 2.3)	2.1 (1.9 to 2.4)	(to)	2.1 (1.9 to 2.3)

Notes:

[23] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[24] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[25] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[26] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	CDR-SB CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1234
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8426
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-0.4
upper limit	0.3

Statistical analysis title	CDR-SB CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D.

	Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1223
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8264
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-0.3
upper limit	0.4

Secondary: [Part I (Base Study)] Percent Change from Baseline in Total Hippocampal Volume (THV)

End point title	[Part I (Base Study)] Percent Change from Baseline in Total Hippocampal Volume (THV)

End point description:

Least squares mean percent CFB at week 78 was calculated for Total Hippocampal Volume (THV) as measured by volumetric magnetic resonance imaging (vMRI). Longitudinal analysis of within-participant THV is computed using a change analysis algorithm using tensor-based morphometry. This technique produces one measure of volume change calculated from the registration of serial vMRI scans at the follow-up time point relative to baseline. Negative percent changes from baseline indicate decreases in THV (i.e. increased hippocampal atrophy). Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose observation for THV (FAS population).

End point type	Secondary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	308[27]	281[28]	0[29]	308[30]
Units: Percent Change				
least squares mean (confidence interval 95%)	-5.6 (-5.9 to -5.4)	-5.7 (-5.9 to -5.4)	(to)	-5.0 (-5.2 to -4.7)

Notes:

[27] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[28] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[29] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[30] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	THV CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D.

	Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	616
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0005
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.6
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-1
upper limit	-0.2

Statistical analysis title	THV CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.7
Confidence interval	
level	Other: 97.51 %
sides	2-sided
lower limit	-1.1
upper limit	-0.3

Secondary: [Part I (Base Study)] Fold Change from Baseline in Cerebrospinal Fluid (CSF) Total Tau

End point title	[Part I (Base Study)] Fold Change from Baseline in Cerebrospinal Fluid (CSF) Total Tau

End point description:

Least squares mean fold CFB at week 78 was calculated for Total Tau concentration in CSF, a measure of brain tau pathology. Per protocol, CSF Total Tau concentration was analyzed as part of a substudy in Part I, with testing occurring only at select trial sites. Least squares mean fold change from baseline >1 indicates increased Total Tau concentration in the CSF. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose observation for CSF Total Tau (FAS population).

End point type	Secondary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32[31]	46[32]	0[33]	33[34]
Units: Fold Change				
least squares mean (confidence interval 95%)	1.02 (0.96 to 1.08)	1.04 (0.99 to 1.09)	(to)	1.07 (1.01 to 1.13)

Notes:

[31] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[32] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[33] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[34] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	Total Tau CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2138
Method	Longitudinal ANCOVA
Parameter estimate	Ratio of Fold Change from Baseline
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.04

Statistical analysis title	Total Tau CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.433
Method	Longitudinal ANCOVA
Parameter estimate	Ratio of Fold Change from Baseline
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.05

Secondary: [Part I (Base Study)] Change from Baseline in Cortical Amyloid Load assessed by [18F]Flutemetamol PET Standard Uptake Value Ratio (SUVR)

End point title	[Part I (Base Study)] Change from Baseline in Cortical Amyloid Load assessed by [18F]Flutemetamol PET Standard Uptake Value Ratio (SUVR)

End point description:

Least squares mean CFB at week 78 was calculated for SUVR, a measure of brain cortical amyloid load. Per protocol, SUVR was analyzed as part of a substudy in Part I, with testing occurring only at select trial sites. Participants receive the PET tracer [18F]Flutemetamol (IV) and, after 90 minutes, receive 4 PET scans (5 minutes each in duration). Using these PET scan images, brain ROIs (frontal, temporal, and parietal lobes; anterior and posterior cingulate and precuneus) are used to calculate regional SUVRs, defined as the relative ratio of pixel intensities at a ROI compared to RR (subcortical white matter). Regional SUVRs are averaged to compute a composite cortical SUVR for each participant. Higher composite cortical SUVR values indicate increased amyloid load, with negative changes indicating decreases in brain amyloid load. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose SUVR observation (FAS population).

End point type	Secondary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20[35]	10[36]	0[37]	14[38]
Units: SUVR				
least squares mean (confidence interval 95%)	-0.02 (-0.04 to -0.01)	-0.04 (-0.06 to -0.03)	(to)	0.00 (-0.01 to 0.01)

Notes:

[35] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[36] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[37] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[38] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	SUVR CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0066
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0

Statistical analysis title	SUVR CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	-0.02

Secondary: [Part I (Base Study)] Percentage of Participants Achieving Responder Status

End point title	[Part I (Base Study)] Percentage of Participants Achieving Responder Status

End point description:

The percentage of participants achieving responder status at week 78 was assessed. To determine which participants were considered responders, a linear regression was conducted at the participant level, yielding an estimated 78-week rate of change (i.e., a slope) for each participant with respect to ADAS-Cog and ADCS-ADL. To be declared a responder, a participant must have: 1) ADAS-Cog and ADCS-ADL observations at baseline and 78 weeks of treatment; 2) an ADAS-Cog slope > 4.0 over 78 weeks, and 3) an ADCS-ADL slope > -6.3 over 78 weeks. A participant failing to meet any of these criteria was designated as a non-responder at Week 78. Analysis population: All randomized participants in Part I receiving ≥1 dose of trial treatment.

End point type	Secondary

End point timeframe:

Week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	652[39]	652[40]	0[41]	653[42]
Units: Percentage of Participants				

number (not applicable)	20.1	19.6		19.3

Notes:

[39] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[40] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[41] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[42] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

No statistical analyses for this end point

Secondary: [Part I (Base Study)] Change from Baseline in Neuropsychiatric Inventory (NPI) Score

End point title	[Part I (Base Study)] Change from Baseline in Neuropsychiatric Inventory (NPI) Score

End point description:

Least squares mean CFB at week 78 was assessed for NPI score. NPI is a clinical assessment of psychiatric status covering 12 domains: delusion; hallucination; agitation/aggression; depression/dysphoria; anxiety; elation/euphoria; apathy/indifference; disinhibition; irritability/lability; aberrant motor behavior; sleep/nighttime behavior; and appetite/eating disorders. Based on interview of participant's caregiver, domains are scored for symptom frequency [range: 1 (occasional) to 4 (very frequent)] and severity [range: 1 (mild) to 3 (severe)]. Frequency and severity scores are multiplied (frequency x severity) to compute domain scores [range: 0 (no symptoms) to 12] The 12 domain scores sum to total NPI score [range: 0-144]. Higher scores reflect more severe psychiatric impairment, with increased impairment reflected by increased NPI score. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose NPI observation (FAS population).

End point type	Secondary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	632[43]	631[44]	0[45]	639[46]
Units: Score on a Scale				
least squares mean (confidence interval 95%)	3.4 (2.5 to 4.4)	3.8 (2.8 to 4.8)	(to)	2.7 (1.7 to 3.7)

Notes:

[43] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[44] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[45] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[46] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	NPI CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]

Number of subjects included in analysis	1271
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2949
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	2.1

Statistical analysis title	NPI CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1270
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1372
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	2.6

Secondary: [Part I (Base Study)] Change from Baseline in Mini-Mental State Examination (MMSE) Score

End point title	[Part I (Base Study)] Change from Baseline in Mini-Mental State Examination (MMSE) Score

End point description:

Least squares mean CFB at week 78 was assessed for MMSE score. MMSE is a cognitive assessment of 5 domains: orientation; attention; memory; language; and constructional praxis. These domains are assessed over the course of 11 total questions related to the participant. Participants are scored based on the number of correct responses; depending on the question, potential scores range from 0 (no correct response) to either 1 (4 questions), 2 (1 question), 3 (3 questions), or 5 (3 questions). Scores from each question are summed to the total MMSE score, with total scores ranging from 0-30. Higher scores indicate better cognitive performance. Further, deterioration in cognitive performance would be reflected by decreases in MMSE score. Analysis population: all randomized participants with a baseline and ≥1 within-analysis-window, post-dose MMSE observation (FAS population).

End point type	Secondary

End point timeframe:

Baseline and week 78

End point values	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II]	Arm C. Verubecestat 60mg/40mg [Part I]; 40 mg [Part II]	Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	610[47]	600[48]	0[49]	628[50]
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-3.9 (-4.3 to -3.6)	-3.6 (-4.0 to -3.3)	(to)	-4.1 (-4.5 to -3.8)

Notes:

[47] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[48] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[49] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

[50] - Per protocol, analysis excludes 200 participants enrolled before IA (all arms) and all in Arm C.

Statistical analyses

Statistical analysis title	MMSE CFB: Verubecestat 12 mg vs. Placebo
Comparison groups	Arm A. Verubecestat 12 mg [Part I]; 12 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1238
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4721
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.7

Statistical analysis title	MMSE CFB: Verubecestat 40 mg vs. Placebo
Comparison groups	Arm B. Verubecestat 40 mg [Part I]; 40 mg [Part II] v Arm D. Placebo [Part I]; Verubecestat 40 mg [Part II]
Number of subjects included in analysis	1228
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0599
Method	Longitudinal ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1

Adverse events information

Timeframe for reporting adverse events:

[Part I]: Up to week 80 of Part I (up to 2 weeks following cessation of study treatment in Part I);
[Part II]: From week 78 (end of treatment in Part I) up to week 262 of Study Part II

Adverse event reporting additional description:

[Part I] Includes all randomized participants in Study Part I (Base Study) receiving ≥1 dose of trial treatment. [Part II] Includes all randomized participants continuing to Study Part II (Extension Study) receiving ≥1 dose of trial treatment in Part II. For Part II-specific arms, only the AEs occurring during study Part II are reported.

Assessment type	Systematic

Dictionary used

Dictionary name	20.0
Dictionary version	20.0

Reporting groups

Reporting group title	Arm A. Verubecestat 12 mg [Part I]

Reporting group description:

[Part I] Verubecestat 12 mg once daily for 78 weeks in Study Part I (Base Study).

Reporting group title	Arm B. Verubecestat 40 mg [Part I]

Reporting group description:

[Part I] Verubecestat 40 mg once daily for 78 weeks in Study Part I (Base Study).

Reporting group title	Arm C. Verubecestat 60mg/40mg [Part I]

Reporting group description:

[Part I] Verubecestat 60 mg once daily until the first IA in Study Part I (Base Study). Following IA, participants in this group were switched to Verubecestat 40 mg once daily, for the remainder of Study Part I (total dosing period: 78 weeks).

Reporting group title	Arm D. Placebo [Part I]

Reporting group description:

[Part I] Placebo once daily for 78 weeks in Study Part I (Base Study).

Reporting group title	Arm A. Verubecestat 12 mg [Part II]

Reporting group description:

[Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 12 mg once daily for an additional 260 weeks.

Reporting group title	Arm B. Verubecestat 40 mg [Part II]

Reporting group description:

[Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Reporting group title	Arm C. Verubecestat 40 mg [Part II]

Reporting group description:

[Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Reporting group title	Arm D. Verubecestat 40 mg [Part II]

Reporting group description:

[Part II] Participants completing Study Part I and continuing to Study Part II (Extension Study) receive Verubecestat 40 mg once daily for an additional 260 weeks.

Serious adverse events	Arm A. Verubecestat 12 mg [Part I]	Arm B. Verubecestat 40 mg [Part I]	Arm C. Verubecestat 60mg/40mg [Part I]
Total subjects affected by serious adverse events			
subjects affected / exposed	134 / 702 (19.09%)	162 / 700 (23.14%)	24 / 103 (23.30%)
number of deaths (all causes)	9	13	3
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Atypical fibroxanthoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
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	9 / 702 (1.28%)	9 / 700 (1.29%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 11	0 / 14	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Bladder transitional cell carcinoma stage II			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Borderline mucinous tumour of ovary			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Bowen's disease			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	0 / 103 (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
Breast cancer			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Breast cancer recurrent			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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 adenoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Extradural neoplasm			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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 cancer			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Glioma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hepatic cancer			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Kaposi's sarcoma			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Keratoacanthoma			
subjects affected / exposed	1 / 702 (0.14%)	3 / 700 (0.43%)	0 / 103 (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
Lentigo maligna			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Lung cancer metastatic			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Lymphoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Malignant melanoma in situ			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of renal pelvis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Metastases to bone			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Metastatic malignant melanoma			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Myelofibrosis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Neuroendocrine tumour			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Ovarian cancer			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Pancreatic carcinoma			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Plasma cell myeloma			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Prostate cancer			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Prostate cancer metastatic			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Prostatic adenoma			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Sarcoma uterus			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Skin squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Small intestine carcinoma			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Squamous cell carcinoma			

subjects affected / exposed	5 / 702 (0.71%)	3 / 700 (0.43%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	1 / 5	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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 skin			
subjects affected / exposed	3 / 702 (0.43%)	2 / 700 (0.29%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Arteriosclerosis			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Deep vein thrombosis			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Venous thrombosis limb			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Asthenia			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Chest discomfort			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Chest pain			
subjects affected / exposed	1 / 702 (0.14%)	4 / 700 (0.57%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Drowning			
subjects affected / exposed	1 / 702 (0.14%)	2 / 700 (0.29%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 2	0 / 0
Euthanasia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Gait disturbance			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Incarcerated hernia			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Malaise			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Mass			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Pyrexia			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hypersensitivity			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Reproductive system and breast disorders			

Benign prostatic hyperplasia			
subjects affected / exposed	3 / 702 (0.43%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast pain			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Cystocele			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Prostatitis			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Prostatomegaly			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Rectocele			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Bronchitis chronic			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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

Bronchospasm			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Noninfective bronchitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Organising pneumonia			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Pharyngeal pouch			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Pleural effusion			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Pneumothorax			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Pneumothorax spontaneous			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Pulmonary embolism			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Pulmonary fibrosis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 702 (0.14%)	2 / 700 (0.29%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Agitation			
subjects affected / exposed	4 / 702 (0.57%)	4 / 700 (0.57%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 5	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Completed suicide			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Delirium			
subjects affected / exposed	0 / 702 (0.00%)	4 / 700 (0.57%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	2 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Delusional disorder, persecutory type			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Delusional disorder, unspecified type			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Depression			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Disorientation			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Emotional distress			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hallucination			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Hallucination, auditory			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Hallucination, visual			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Major depression			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Mental status changes			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric symptoms			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Paranoia			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Psychogenic movement disorder			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Psychotic disorder			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Restlessness			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Sleep disorder			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Suicidal behaviour			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Suicidal ideation			
subjects affected / exposed	2 / 702 (0.28%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ammonia increased			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose decreased			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose fluctuation			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Heart rate irregular			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hepatic enzyme increased			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Lipoprotein (a) increased			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Liver function test increased			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Prostatic specific antigen increased			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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			
Accidental overdose			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Anastomotic leak			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Ankle fracture			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Carbon monoxide poisoning			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Cervical vertebral fracture			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Comminuted fracture			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Concussion			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Contusion			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Facial bones fracture			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Fall			
subjects affected / exposed	3 / 702 (0.43%)	1 / 700 (0.14%)	0 / 103 (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
Femoral neck fracture			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Femur fracture			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Foot fracture			

subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Fracture displacement			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Hand fracture			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Head injury			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 702 (0.00%)	5 / 700 (0.71%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	0 / 103 (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
Joint dislocation			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Laceration			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Lumbar vertebral fracture			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Meniscus injury			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Multiple fractures			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Muscle strain			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prescribed overdose			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Radius fracture			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Rib fracture			
subjects affected / exposed	1 / 702 (0.14%)	2 / 700 (0.29%)	0 / 103 (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
Skin abrasion			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Spinal compression fracture			

subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Spinal fracture			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Subdural haematoma			
subjects affected / exposed	2 / 702 (0.28%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Subdural haemorrhage			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Thermal burn			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Tibia fracture			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Toxicity to various agents			

subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Traumatic fracture			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Vaccination complication			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Angina unstable			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Atrial fibrillation			

subjects affected / exposed	3 / 702 (0.43%)	2 / 700 (0.29%)	3 / 103 (2.91%)
occurrences causally related to treatment / all	0 / 3	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Cardiac arrest			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Cardiac failure			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Coronary artery disease			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Coronary artery occlusion			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Mitral valve incompetence			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Myocardial infarction			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Myocardial ischaemia			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Pericardial effusion			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Pericarditis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Sinus bradycardia			
subjects affected / exposed	1 / 702 (0.14%)	2 / 700 (0.29%)	0 / 103 (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
Sinus node dysfunction			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Stress cardiomyopathy			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Torsade de pointes			

subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Conduction disorder			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Ataxia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Carotid artery occlusion			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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 infarction			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Cerebral infarction			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Cerebrovascular accident			
subjects affected / exposed	2 / 702 (0.28%)	6 / 700 (0.86%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cognitive disorder			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Dementia			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Dementia Alzheimer's type			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Depressed level of consciousness			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Diplegia			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Dizziness			
subjects affected / exposed	2 / 702 (0.28%)	2 / 700 (0.29%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Epilepsy			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Headache			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Ischaemic stroke			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Loss of consciousness			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Memory impairment			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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 encephalopathy			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Paraesthesia			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Partial seizures			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Presyncope			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor skills impaired			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Radiculopathy			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Sciatica			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Seizure			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Somnolence			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Syncope			

subjects affected / exposed	7 / 702 (1.00%)	13 / 700 (1.86%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 7	2 / 15	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	3 / 702 (0.43%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic anaemia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Leukocytosis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Neutropenia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Meniere's disease			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Vertigo positional			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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			
Cataract			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Corneal oedema			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Glaucoma			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Keratitis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Macular oedema			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Retinal detachment			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Trichiasis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Abdominal pain lower			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Abdominal pain upper			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal prolapse			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Colitis			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Diarrhoea			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	0 / 103 (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
Diverticulum			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Diverticulum oesophageal			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Dysphagia			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Faecaloma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Gastric ulcer			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Haemorrhoids			

subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Ileus			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Inguinal hernia			
subjects affected / exposed	1 / 702 (0.14%)	2 / 700 (0.29%)	0 / 103 (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
Intestinal obstruction			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Large intestine perforation			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Melaena			

subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Nausea			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal spasm			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Oesophagitis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Pancreatitis acute			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Retroperitoneal haematoma			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Vomiting			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	0 / 103 (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
Biliary colic			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Cholangitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Cholangitis acute			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Cholecystitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Cholecystitis chronic			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Cholelithiasis			

subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Hepatic cyst			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Hepatitis acute			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Jaundice			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Dermal cyst			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Erythema			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Petechiae			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
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 macular			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
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 maculo-papular			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Urticaria			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Bladder spasm			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
End stage renal disease			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Haematuria			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Incontinence			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	2 / 702 (0.28%)	1 / 700 (0.14%)	0 / 103 (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
Renal colic			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Stress urinary incontinence			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Ureterolithiasis			
subjects affected / exposed	2 / 702 (0.28%)	1 / 700 (0.14%)	0 / 103 (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
Urethral disorder			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Urethral stenosis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Urinary incontinence			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Urinary retention			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Endocrine disorders			
Thyroid cyst			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropathy			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Back pain			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Fracture pain			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Gouty arthritis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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

Haemarthrosis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Muscle spasms			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Myalgia			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Neck pain			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Osteoarthritis			
subjects affected / exposed	1 / 702 (0.14%)	3 / 700 (0.43%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Tendonitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Anal abscess			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Appendicitis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Bacteraemia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Bronchitis			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Cellulitis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Cystitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Diverticulitis			

subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Erysipelas			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder empyema			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Gastroenteritis			
subjects affected / exposed	0 / 702 (0.00%)	2 / 700 (0.29%)	0 / 103 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Haematoma infection			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Helicobacter gastritis			

subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Influenza			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Meningoencephalitis herpetic			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Neurosyphilis			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Osteomyelitis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Otitis media acute			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Periorbital cellulitis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Peritonitis			

subjects affected / exposed	2 / 702 (0.28%)	0 / 700 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 702 (0.71%)	6 / 700 (0.86%)	3 / 103 (2.91%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Retroperitoneal infection			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Sepsis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Tuberculous pleurisy			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Urinary tract infection			

subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	3 / 702 (0.43%)	1 / 700 (0.14%)	0 / 103 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Dehydration			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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
Diabetes mellitus			
subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Failure to thrive			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 702 (0.14%)	1 / 700 (0.14%)	0 / 103 (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
Hypoglycaemia			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hypokalaemia			

subjects affected / exposed	1 / 702 (0.14%)	0 / 700 (0.00%)	0 / 103 (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
Hypokalaemic syndrome			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Hyponatraemia			
subjects affected / exposed	0 / 702 (0.00%)	3 / 700 (0.43%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	1 / 702 (0.14%)	2 / 700 (0.29%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Starvation			
subjects affected / exposed	0 / 702 (0.00%)	0 / 700 (0.00%)	0 / 103 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 702 (0.00%)	1 / 700 (0.14%)	0 / 103 (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

Serious adverse events	Arm D. Placebo [Part I]	Arm A. Verubecestat 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part II]
Total subjects affected by serious adverse events			
subjects affected / exposed	121 / 705 (17.16%)	57 / 379 (15.04%)	56 / 365 (15.34%)
number of deaths (all causes)	6	6	4
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Atypical fibroxanthoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Basal cell carcinoma			
subjects affected / exposed	15 / 705 (2.13%)	2 / 379 (0.53%)	3 / 365 (0.82%)
occurrences causally related to treatment / all	0 / 17	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Bladder transitional cell carcinoma stage II			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Borderline mucinous tumour of ovary			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Bowen's disease			
subjects affected / exposed	3 / 705 (0.43%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Breast cancer			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 recurrent			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cholangiocarcinoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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 adenoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Colon cancer			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural neoplasm			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Gastric cancer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Glioma			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hepatic cancer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Kaposi's sarcoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Keratoacanthoma			
subjects affected / exposed	3 / 705 (0.43%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lentigo maligna			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Lung adenocarcinoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Lung cancer metastatic			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Lymphoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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	3 / 705 (0.43%)	1 / 379 (0.26%)	0 / 365 (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
Malignant melanoma in situ			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of renal pelvis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 bone			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Metastatic malignant melanoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Metastatic squamous cell carcinoma			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelofibrosis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Neuroendocrine tumour			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Ovarian cancer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Plasma cell myeloma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Prostate cancer metastatic			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Rectal cancer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Sarcoma uterus			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Skin squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestine carcinoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Squamous cell carcinoma			
subjects affected / exposed	3 / 705 (0.43%)	5 / 379 (1.32%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Squamous cell carcinoma of lung			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	4 / 705 (0.57%)	1 / 379 (0.26%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Uterine cancer			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Arteriosclerosis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Hypotension			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hypovolaemic shock			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Venous thrombosis limb			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	2 / 705 (0.28%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Chest pain			

subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Drowning			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Euthanasia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Gait disturbance			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Incarcerated hernia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Malaise			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Mass			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Non-cardiac chest pain			
subjects affected / exposed	2 / 705 (0.28%)	0 / 379 (0.00%)	0 / 365 (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
Pyrexia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hypersensitivity			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 pain			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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

Cystocele			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Prostatitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Prostatomegaly			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Rectocele			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Bronchospasm			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Noninfective bronchitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Organising pneumonia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Pharyngeal pouch			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Pleural effusion			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Pneumothorax			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Pneumothorax spontaneous			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Pulmonary embolism			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	2 / 705 (0.28%)	0 / 379 (0.00%)	0 / 365 (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
Aggression			
subjects affected / exposed	2 / 705 (0.28%)	1 / 379 (0.26%)	0 / 365 (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
Agitation			
subjects affected / exposed	0 / 705 (0.00%)	5 / 379 (1.32%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Confusional state			

subjects affected / exposed	3 / 705 (0.43%)	2 / 379 (0.53%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Delusion			
subjects affected / exposed	0 / 705 (0.00%)	2 / 379 (0.53%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusional disorder, persecutory type			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusional disorder, unspecified type			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Depression			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Disorientation			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Emotional distress			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hallucination			

subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Hallucination, auditory			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hallucination, visual			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 705 (0.14%)	3 / 379 (0.79%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric symptoms			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Paranoia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Psychogenic movement disorder			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Psychotic disorder			

subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Restlessness			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Sleep disorder			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Suicidal behaviour			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Ammonia increased			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose decreased			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose fluctuation			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Heart rate irregular			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
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	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Lipoprotein (a) increased			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Liver function test increased			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Prostatic specific antigen increased			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Anastomotic leak			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Ankle fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbon monoxide poisoning			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cervical vertebral fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Comminuted fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Concussion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Contusion			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Facial bones fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Fall			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Femur fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Foot fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Fracture displacement			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Hand fracture			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Head injury			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hip fracture			
subjects affected / exposed	1 / 705 (0.14%)	2 / 379 (0.53%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Joint dislocation			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Laceration			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Lumbar vertebral fracture			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Meniscus injury			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Multiple fractures			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Prescribed overdose			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Radius fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Rib fracture			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Skin abrasion			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Spinal compression fracture			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Spinal fracture			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Thermal burn			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 705 (0.00%)	2 / 379 (0.53%)	0 / 365 (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
Tibia fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Toxicity to various agents			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Traumatic fracture			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
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 intracranial haemorrhage			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Vaccination complication			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Acute myocardial infarction			
subjects affected / exposed	2 / 705 (0.28%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Atrial fibrillation			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 failure			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure congestive			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Coronary artery disease			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery occlusion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Mitral valve incompetence			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Myocardial infarction			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Pericardial effusion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Pericarditis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Sinus bradycardia			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Sinus node dysfunction			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Stress cardiomyopathy			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Torsade de pointes			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Conduction disorder			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Ataxia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery occlusion			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cerebellar infarction			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cerebral infarction			
subjects affected / exposed	1 / 705 (0.14%)	1 / 379 (0.26%)	0 / 365 (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
Cerebrovascular accident			
subjects affected / exposed	4 / 705 (0.57%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Dementia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Dementia Alzheimer's type			

subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Depressed level of consciousness			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Diplegia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Dizziness			
subjects affected / exposed	3 / 705 (0.43%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Epilepsy			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Facial paralysis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Intracranial aneurysm			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Ischaemic stroke			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Loss of consciousness			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbosacral radiculopathy			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Memory impairment			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Paraesthesia			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Partial seizures			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Presyncope			

subjects affected / exposed	0 / 705 (0.00%)	3 / 379 (0.79%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor skills impaired			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Radiculopathy			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Sciatica			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Seizure			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	2 / 705 (0.28%)	0 / 379 (0.00%)	0 / 365 (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
Syncope			
subjects affected / exposed	5 / 705 (0.71%)	1 / 379 (0.26%)	3 / 365 (0.82%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
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	0 / 705 (0.00%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic anaemia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Leukocytosis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Neutropenia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Meniere's disease			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Vertigo positional			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Eye disorders			
Cataract			
subjects affected / exposed	2 / 705 (0.28%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corneal oedema			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Glaucoma			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Keratitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Macular oedema			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Retinal detachment			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Trichiasis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Abdominal pain lower			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Abdominal pain upper			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Anal prolapse			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Colitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Diverticulum			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Diverticulum oesophageal			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Dysphagia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Haematemesis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Haemorrhoids			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Ileus			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Incarcerated umbilical hernia			

subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Inguinal hernia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Intestinal obstruction			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Melaena			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Nausea			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal spasm			

subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Oesophagitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Pancreatitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Retroperitoneal haematoma			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Vomiting			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Biliary colic			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cholangitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Cholangitis acute			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cholecystitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 chronic			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Cholelithiasis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hepatitis acute			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Jaundice			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Dermal cyst			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Erythema			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Petechiae			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Rash macular			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Rash maculo-papular			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Urticaria			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Bladder spasm			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Calculus bladder			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
End stage renal disease			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Haematuria			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Incontinence			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Nephrolithiasis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
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 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Stress urinary incontinence			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Ureterolithiasis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral disorder			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Urethral stenosis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Urinary retention			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Endocrine disorders			
Thyroid cyst			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropathy			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Back pain			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture pain			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Gouty arthritis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Muscle spasms			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Myalgia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Neck pain			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 705 (0.43%)	1 / 379 (0.26%)	0 / 365 (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
Spinal column stenosis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Tendonitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Bacteraemia			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Bronchitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Bronchitis viral			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cellulitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Cystitis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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	0 / 705 (0.00%)	2 / 379 (0.53%)	0 / 365 (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
Erysipelas			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Escherichia urinary tract infection			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Gallbladder empyema			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Gastroenteritis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Haematoma infection			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Helicobacter gastritis			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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
Influenza			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Meningoencephalitis herpetic			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Neurosyphilis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Osteomyelitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Otitis media acute			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Periorbital cellulitis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Peritonitis			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Pneumonia			
subjects affected / exposed	5 / 705 (0.71%)	3 / 379 (0.79%)	5 / 365 (1.37%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Pyelonephritis			

subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Streptococcal sepsis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Tuberculous pleurisy			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Urinary tract infection			
subjects affected / exposed	2 / 705 (0.28%)	2 / 379 (0.53%)	1 / 365 (0.27%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 705 (0.28%)	1 / 379 (0.26%)	0 / 365 (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
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Dehydration			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	3 / 365 (0.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Failure to thrive			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hypercalcaemia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hypoglycaemia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hypokalaemia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Hypokalaemic syndrome			
subjects affected / exposed	0 / 705 (0.00%)	1 / 379 (0.26%)	0 / 365 (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	0 / 705 (0.00%)	0 / 379 (0.00%)	2 / 365 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Metabolic acidosis			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (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
Starvation			
subjects affected / exposed	1 / 705 (0.14%)	0 / 379 (0.00%)	0 / 365 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 705 (0.00%)	0 / 379 (0.00%)	0 / 365 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm C. Verubecestat 40 mg [Part II]	Arm D. Verubecestat 40 mg [Part II]	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 61 (36.07%)	69 / 394 (17.51%)	
number of deaths (all causes)	4	8	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atypical fibroxanthoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma stage II			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Borderline mucinous tumour of ovary			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon adenoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural neoplasm			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glioma			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intraductal proliferative breast lesion			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kaposi's sarcoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of renal pelvis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sarcoma uterus			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine carcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	2 / 61 (3.28%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 lung			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 skin			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			

subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Adverse drug reaction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drowning			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Euthanasia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gait disturbance			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 61 (0.00%)	3 / 394 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Anaphylactic reaction			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Prostatomegaly			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Noninfective bronchitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pharyngeal pouch			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 61 (1.64%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sleep apnoea syndrome			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aggression			
subjects affected / exposed	0 / 61 (0.00%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	1 / 61 (1.64%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusion			

subjects affected / exposed	1 / 61 (1.64%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusional disorder, persecutory type			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusional disorder, unspecified type			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emotional distress			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	1 / 61 (1.64%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, auditory			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropsychiatric symptoms			
subjects affected / exposed	0 / 61 (0.00%)	3 / 394 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranoia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychogenic movement disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restlessness			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep disorder			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal behaviour			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ammonia increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose decreased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose fluctuation			

subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate irregular			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoprotein (a) increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Accidental overdose			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic leak			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 61 (0.00%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	2 / 61 (3.28%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prescribed overdose			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin abrasion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaccination complication			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	0 / 61 (0.00%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conduction disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Amnesia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 61 (0.00%)	5 / 394 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 3	
Depressed level of consciousness			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplegia			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			

subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychomotor skills impaired			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 61 (1.64%)	3 / 394 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	2 / 61 (3.28%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 61 (1.64%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 61 (3.28%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniere's disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal oedema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular oedema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trichiasis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 61 (0.00%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal prolapse			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	3 / 394 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum oesophageal			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			

subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cyst			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Decubitus ulcer			

subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petechiae			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder spasm			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incontinence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 61 (1.64%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroid cyst			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Arthralgia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 61 (3.28%)	2 / 394 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Anal abscess			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis herpetic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	3 / 61 (4.92%)	4 / 394 (1.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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			
Decreased appetite			
subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			

subjects affected / exposed	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypercalcaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemic syndrome			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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 / 61 (0.00%)	1 / 394 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (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	1 / 61 (1.64%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Starvation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 61 (0.00%)	0 / 394 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A. Verubecestat 12 mg [Part I]	Arm B. Verubecestat 40 mg [Part I]	Arm C. Verubecestat 60mg/40mg [Part I]
Total subjects affected by non-serious adverse events			
subjects affected / exposed	408 / 702 (58.12%)	440 / 700 (62.86%)	66 / 103 (64.08%)
Investigations			
Weight decreased			
subjects affected / exposed	47 / 702 (6.70%)	44 / 700 (6.29%)	7 / 103 (6.80%)
occurrences (all)	48	44	7
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	25 / 702 (3.56%)	30 / 700 (4.29%)	7 / 103 (6.80%)
occurrences (all)	31	33	9
Fall			
subjects affected / exposed	56 / 702 (7.98%)	59 / 700 (8.43%)	8 / 103 (7.77%)
occurrences (all)	84	75	8
Nervous system disorders			
Dizziness			
subjects affected / exposed	33 / 702 (4.70%)	56 / 700 (8.00%)	12 / 103 (11.65%)
occurrences (all)	34	70	15
Headache			
subjects affected / exposed	42 / 702 (5.98%)	52 / 700 (7.43%)	5 / 103 (4.85%)
occurrences (all)	48	59	7

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 702 (1.14%)	11 / 700 (1.57%)	1 / 103 (0.97%)
occurrences (all)	8	11	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	30 / 702 (4.27%)	27 / 700 (3.86%)	9 / 103 (8.74%)
occurrences (all)	32	29	9
Diarrhoea			
subjects affected / exposed	56 / 702 (7.98%)	60 / 700 (8.57%)	4 / 103 (3.88%)
occurrences (all)	65	70	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	32 / 702 (4.56%)	26 / 700 (3.71%)	6 / 103 (5.83%)
occurrences (all)	38	27	6
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	33 / 702 (4.70%)	26 / 700 (3.71%)	6 / 103 (5.83%)
occurrences (all)	38	31	6
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	11 / 702 (1.57%)	15 / 700 (2.14%)	6 / 103 (5.83%)
occurrences (all)	11	16	6
Agitation			
subjects affected / exposed	31 / 702 (4.42%)	16 / 700 (2.29%)	5 / 103 (4.85%)
occurrences (all)	32	17	7
Anxiety			
subjects affected / exposed	40 / 702 (5.70%)	47 / 700 (6.71%)	8 / 103 (7.77%)
occurrences (all)	41	51	10
Depression			
subjects affected / exposed	47 / 702 (6.70%)	46 / 700 (6.57%)	9 / 103 (8.74%)
occurrences (all)	52	48	9
Insomnia			
subjects affected / exposed	41 / 702 (5.84%)	33 / 700 (4.71%)	6 / 103 (5.83%)
occurrences (all)	42	33	6
Suicidal ideation			

subjects affected / exposed	39 / 702 (5.56%)	45 / 700 (6.43%)	4 / 103 (3.88%)
occurrences (all)	42	55	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	36 / 702 (5.13%)	26 / 700 (3.71%)	4 / 103 (3.88%)
occurrences (all)	41	26	5
Back pain			
subjects affected / exposed	36 / 702 (5.13%)	46 / 700 (6.57%)	6 / 103 (5.83%)
occurrences (all)	39	49	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	24 / 702 (3.42%)	10 / 700 (1.43%)	6 / 103 (5.83%)
occurrences (all)	28	11	7
Urinary tract infection			
subjects affected / exposed	61 / 702 (8.69%)	71 / 700 (10.14%)	15 / 103 (14.56%)
occurrences (all)	79	93	18
Viral upper respiratory tract infection			
subjects affected / exposed	60 / 702 (8.55%)	50 / 700 (7.14%)	5 / 103 (4.85%)
occurrences (all)	81	60	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	19 / 702 (2.71%)	30 / 700 (4.29%)	6 / 103 (5.83%)
occurrences (all)	20	31	7

Non-serious adverse events	Arm D. Placebo [Part I]	Arm A. Verubecestat 12 mg [Part II]	Arm B. Verubecestat 40 mg [Part II]
Total subjects affected by non-serious adverse events			
subjects affected / exposed	337 / 705 (47.80%)	135 / 379 (35.62%)	102 / 365 (27.95%)
Investigations			
Weight decreased			
subjects affected / exposed	21 / 705 (2.98%)	10 / 379 (2.64%)	8 / 365 (2.19%)
occurrences (all)	22	10	8
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	21 / 705 (2.98%)	14 / 379 (3.69%)	8 / 365 (2.19%)
occurrences (all)	27	21	8
Fall			

subjects affected / exposed	39 / 705 (5.53%)	31 / 379 (8.18%)	19 / 365 (5.21%)
occurrences (all)	51	37	25
Nervous system disorders			
Dizziness			
subjects affected / exposed	32 / 705 (4.54%)	9 / 379 (2.37%)	3 / 365 (0.82%)
occurrences (all)	35	9	3
Headache			
subjects affected / exposed	41 / 705 (5.82%)	4 / 379 (1.06%)	5 / 365 (1.37%)
occurrences (all)	58	6	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 705 (0.85%)	5 / 379 (1.32%)	1 / 365 (0.27%)
occurrences (all)	6	5	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	20 / 705 (2.84%)	13 / 379 (3.43%)	3 / 365 (0.82%)
occurrences (all)	20	14	3
Diarrhoea			
subjects affected / exposed	42 / 705 (5.96%)	8 / 379 (2.11%)	8 / 365 (2.19%)
occurrences (all)	45	9	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 705 (3.12%)	7 / 379 (1.85%)	9 / 365 (2.47%)
occurrences (all)	23	9	10
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	25 / 705 (3.55%)	7 / 379 (1.85%)	3 / 365 (0.82%)
occurrences (all)	31	7	3
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	6 / 705 (0.85%)	1 / 379 (0.26%)	1 / 365 (0.27%)
occurrences (all)	6	2	1
Agitation			
subjects affected / exposed	19 / 705 (2.70%)	8 / 379 (2.11%)	5 / 365 (1.37%)
occurrences (all)	20	8	5
Anxiety			

subjects affected / exposed	27 / 705 (3.83%)	6 / 379 (1.58%)	6 / 365 (1.64%)
occurrences (all)	29	6	6
Depression			
subjects affected / exposed	38 / 705 (5.39%)	5 / 379 (1.32%)	6 / 365 (1.64%)
occurrences (all)	38	5	6
Insomnia			
subjects affected / exposed	21 / 705 (2.98%)	12 / 379 (3.17%)	8 / 365 (2.19%)
occurrences (all)	23	12	8
Suicidal ideation			
subjects affected / exposed	24 / 705 (3.40%)	12 / 379 (3.17%)	9 / 365 (2.47%)
occurrences (all)	26	14	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 705 (2.98%)	8 / 379 (2.11%)	7 / 365 (1.92%)
occurrences (all)	23	11	8
Back pain			
subjects affected / exposed	30 / 705 (4.26%)	8 / 379 (2.11%)	7 / 365 (1.92%)
occurrences (all)	34	8	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	19 / 705 (2.70%)	9 / 379 (2.37%)	5 / 365 (1.37%)
occurrences (all)	19	12	5
Urinary tract infection			
subjects affected / exposed	56 / 705 (7.94%)	20 / 379 (5.28%)	18 / 365 (4.93%)
occurrences (all)	68	25	21
Viral upper respiratory tract infection			
subjects affected / exposed	42 / 705 (5.96%)	21 / 379 (5.54%)	11 / 365 (3.01%)
occurrences (all)	49	27	12
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	16 / 705 (2.27%)	4 / 379 (1.06%)	0 / 365 (0.00%)
occurrences (all)	16	4	0

Non-serious adverse events	Arm C. Verubecestat 40 mg [Part II]	Arm D. Verubecestat 40 mg [Part II]	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 61 (60.66%)	144 / 394 (36.55%)	

Investigations			
Weight decreased			
subjects affected / exposed	2 / 61 (3.28%)	13 / 394 (3.30%)	
occurrences (all)	2	13	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 61 (3.28%)	5 / 394 (1.27%)	
occurrences (all)	2	5	
Fall			
subjects affected / exposed	7 / 61 (11.48%)	22 / 394 (5.58%)	
occurrences (all)	14	27	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 61 (1.64%)	8 / 394 (2.03%)	
occurrences (all)	1	10	
Headache			
subjects affected / exposed	2 / 61 (3.28%)	6 / 394 (1.52%)	
occurrences (all)	2	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 61 (6.56%)	5 / 394 (1.27%)	
occurrences (all)	5	5	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 61 (6.56%)	10 / 394 (2.54%)	
occurrences (all)	5	10	
Diarrhoea			
subjects affected / exposed	4 / 61 (6.56%)	9 / 394 (2.28%)	
occurrences (all)	5	10	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 61 (1.64%)	13 / 394 (3.30%)	
occurrences (all)	1	14	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 61 (1.64%)	8 / 394 (2.03%)	
occurrences (all)	1	8	

Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 61 (0.00%)	3 / 394 (0.76%)	
occurrences (all)	0	3	
Agitation			
subjects affected / exposed	5 / 61 (8.20%)	10 / 394 (2.54%)	
occurrences (all)	6	11	
Anxiety			
subjects affected / exposed	6 / 61 (9.84%)	8 / 394 (2.03%)	
occurrences (all)	6	8	
Depression			
subjects affected / exposed	5 / 61 (8.20%)	8 / 394 (2.03%)	
occurrences (all)	5	9	
Insomnia			
subjects affected / exposed	2 / 61 (3.28%)	10 / 394 (2.54%)	
occurrences (all)	2	10	
Suicidal ideation			
subjects affected / exposed	2 / 61 (3.28%)	12 / 394 (3.05%)	
occurrences (all)	2	13	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 61 (8.20%)	3 / 394 (0.76%)	
occurrences (all)	5	3	
Back pain			
subjects affected / exposed	2 / 61 (3.28%)	6 / 394 (1.52%)	
occurrences (all)	3	6	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 61 (3.28%)	4 / 394 (1.02%)	
occurrences (all)	2	5	
Urinary tract infection			
subjects affected / exposed	5 / 61 (8.20%)	28 / 394 (7.11%)	
occurrences (all)	6	34	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 61 (3.28%)	10 / 394 (2.54%)	
occurrences (all)	2	11	

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 61 (1.64%) 1	 10 / 394 (2.54%) 10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2012	Amendment 01: The primary purpose of this amendment was to: 1) include ophthalmologic assessments to monitor for retinal effects and to provide long-term ocular safety data in the Safety and Main Cohorts; 2) exclude the first 200 participants enrolled from the primary efficacy analyses; and 3) clarify the IA process.
20 June 2012	Amendment 02: The primary purpose of this amendment was to add language whereby the external data monitoring committee (eDMC) may recommend reducing or dropping the requirements for MRI monitoring if indicated or increasing the frequency of MRI scans for the Main Cohort if a safety signal emerges in the Safety Cohort.
24 June 2013	Amendment 05: The primary purpose of this amendment was to add ophthalmologic assessments to monitor the iris and potential complications of iris pigment loss in the Safety and Main Cohorts.
10 October 2013	Amendment 07: The primary purpose of this amendment was to: 1) exclude the use of digoxin for all participants; 2) drop the 60 mg Verubecestat dose from the Main Cohort; 3) revise the primary analysis approach, analysis populations, and analytical model; and 4) update trial procedures, monitoring, and guidance.
25 March 2014	Amendment 08: The primary purpose of this amendment was to create and describe a long term, double-blind extension phase (i.e. Part II), outlining study objectives, procedures, and statistical analysis plan for Part II.
19 February 2015	Amendment 10: The primary purpose of this amendment was to: 1) discontinue iris and intraocular pressure monitoring; and 2) remove routine MRI safety monitoring in response to updated Food and Drug Administration (FDA) guidance.
06 May 2015	Amendment 13: The primary purpose of this amendment was to discontinue ophthalmic monitoring and remove opthamology-related exclusion criteria for new participants at the recommendation of the eDMC.
05 August 2016	Amendment 17: The primary purpose of this amendment was to: 1) modify criteria for futility interim analysis; 2) update the statistical analysis plan with respect to sensitivity analysis; and 3) reinstate the collection of plasma pharmacokinetic sampling.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 February 2017	Trial was terminated early	-

Notes:

Limitations and caveats

None reported