Clinical trial results:
A Phase I/II, Open-label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumour Activity of Ascending Doses of AZD9291 (osimertinib) in Patients with Advanced Non-small Cell Lung Cancer who have Progressed Following Prior Therapy with an Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitor Agent (AURA)

Summary

EudraCT number	2012-004628-39
Trial protocol	GB DE IT
Global end of trial date	11 December 2023

Results information

Result version number	v1 (current)
This version publication date	26 December 2024
First version publication date	26 December 2024

Trial information

Trial identification

Sponsor protocol code	D5160C00001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Melbourn Science Park, Cambridge Street, Melbourn, United Kingdom, SG8 6EE
Public contact	Senior Medical Director, Tagrisso, AstraZeneca, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Senior Medical Director, Tagrisso, AstraZeneca, ClinicalTrialTransparency@astrazeneca.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	01 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the AURA study was to investigate the safety, tolerability, and efficacy (objective response rate [ORR]) of osimertinib when given orally to patients with locally advanced or metastatic Non Small Cell Lung Cancer (NSCLC) who have progressed following prior therapy with an Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitor (TKI) agent
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Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonisation / Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	France: 29
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Japan: 102
Country: Number of subjects enrolled	Korea, Republic of: 142
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	Taiwan: 97
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 106
Worldwide total number of subjects	603
EEA total number of subjects	111

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)	378
From 65 to 84 years	219
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Patients recruited to different cohorts. Dose escalation cohort of pre-treated patients in 5 dose groups. Dose expansion cohort (pre-treated) in same 5 dose groups. First line patient cohort. 80mg tablet cohort of pre-treated patients. Japan-only cohort (EGFR T790M+ by cytology). Phase II extension cohort in pre-treated EGFR T790M+ patients.

Pre-assignment

Screening details:

603 patients were enrolled and received treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AZD9291 80mg Extension

Arm description:

Phase II dose extension cohort in pre-treated EGFR T790M mutation positive patients in AZD9291 80mg tablet.

Arm type	Experimental
Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

80mg oral

Arm title	Dose escalation

Arm description:

Pre-treated patient cohort in doses 20, 40, 80, 160 and 240mg AZD9291 capsule.

Arm type	Experimental
Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

20-240mg oral

Arm title	Dose expansion

Arm description:

Pre-treated EGFR T790M mutation positive (by central testing) patient cohort. Dose groups were expanded to include more patients.

Arm type	Experimental

Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

20-240mg oral

Arm title	First line

Arm description:

Cohort of patients receiving first-line treatment for EGFRm advanced NSCLC, in 80mg and 160mg AZD9291 capsule.

Arm type	Experimental
Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

80-160mg oral

Arm title	80mg tablet

Arm description:

US-only cohort of pre-treated EGFR patients receiving the tablet formulation of AZD9291 (80 mg).

Arm type	Experimental
Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

80mg oral

Arm title	Japan cytology

Arm description:

Japan-only cohort of patients (EGFR T790M mutation status determined from cytology samples) receiving AZD9291 80 mg tablet.

Arm type	Experimental
Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

80mg oral

Number of subjects in period 1	AZD9291 80mg Extension	Dose escalation	Dose expansion
Started	201	31	271
Completed	0	0	0
Not completed	201	31	271
Adverse event, serious fatal	135	5	52
Consent withdrawn by subject	15	2	15
Terminated due to study closure	46	-	-
Objective Disease Progression	-	18	164
Other (not specified)	1	-	8
Lost to follow-up	4	-	-
Ongoing Study at Data Cut-off	-	6	32

Number of subjects in period 1	First line	80mg tablet	Japan cytology
Started	60	12	28
Completed	0	0	0
Not completed	60	12	28
Adverse event, serious fatal	5	4	2
Consent withdrawn by subject	5	1	1
Terminated due to study closure	11	-	-
Objective Disease Progression	35	7	17
Other (not specified)	3	-	1
Lost to follow-up	1	-	-
Ongoing Study at Data Cut-off	-	-	7

Baseline characteristics

Reporting groups	
Reporting group title	AZD9291 80mg Extension
Reporting group description:	
Phase II dose extension cohort in pre-treated EGFR T790M mutation positive patients in AZD9291 80mg tablet.	
Reporting group title	Dose escalation
Reporting group description:	
Pre-treated patient cohort in doses 20, 40, 80, 160 and 240mg AZD9291 capsule.	
Reporting group title	Dose expansion
Reporting group description:	
Pre-treated EGFR T790M mutation positive (by central testing) patient cohort. Dose groups were expanded to include more patients.	
Reporting group title	First line
Reporting group description:	
Cohort of patients receiving first-line treatment for EGFRm advanced NSCLC, in 80mg and 160mg AZD9291 capsule.	
Reporting group title	80mg tablet
Reporting group description:	
US-only cohort of pre-treated EGFR patients receiving the tablet formulation of AZD9291 (80 mg).	
Reporting group title	Japan cytology
Reporting group description:	
Japan-only cohort of patients (EGFR T790M mutation status determined from cytology samples) receiving AZD9291 80 mg tablet.	

Reporting group values	AZD9291 80mg Extension	Dose escalation	Dose expansion
Number of subjects	201	31	271
Age, Customized Units: Subjects			
<50 Years|	30	3	42
>=50-<65 Years|	86	19	142
>=65-<75 Years|	64	8	59
>=75 Years|	21	1	28
Age continuous Units: years			
arithmetic mean	61.4	59.8	60.0
standard deviation	± 10.58	± 8.8	± 10.7
Gender, Male/Female Units: Subjects			
Female	133	20	167
Male	68	11	104
Race, Customized Units: Subjects			
Asian|	114	21	160
Black Or African American|	1	0	3
Missing|	2	0	0
Not Reported|	4	4	11
Other|	4	0	0
White|	76	6	96

American Indian or Alaska Native|	0	0	1

Reporting group values	First line	80mg tablet	Japan cytology
Number of subjects	60	12	28
Age, Customized Units: Subjects			
<50 Years|	8	3	3
>=50-<65 Years|	23	6	13
>=65-<75 Years|	22	3	9
>=75 Years|	7	0	3
Age continuous Units: years			
arithmetic mean	62.1	57.6	62.4
standard deviation	± 10.8	± 9.8	± 9.7
Gender, Male/Female Units: Subjects			
Female	45	8	21
Male	15	4	7
Race, Customized Units: Subjects			
Asian|	43	4	28
Black Or African American|	0	1	0
Missing|	0	0	0
Not Reported|	1	0	0
Other|	0	0	0
White|	15	7	0
American Indian or Alaska Native|	1	0	0

Reporting group values	Total		
Number of subjects	603		
Age, Customized Units: Subjects			
<50 Years|	89		
>=50-<65 Years|	289		
>=65-<75 Years|	165		
>=75 Years|	60		
Age continuous Units: years arithmetic mean standard deviation	- 		
Gender, Male/Female Units: Subjects			
Female	394		
Male	209		
Race, Customized Units: Subjects			
Asian|	370		
Black Or African American|	5		
Missing|	2		

Not Reported|	20		
Other|	4		
White|	200		
American Indian or Alaska Native|	2		

End points

End points reporting groups

Reporting group title	AZD9291 80mg Extension
Reporting group description:	
Phase II dose extension cohort in pre-treated EGFR T790M mutation positive patients in AZD9291 80mg tablet.	
Reporting group title	Dose escalation
Reporting group description:	
Pre-treated patient cohort in doses 20, 40, 80, 160 and 240mg AZD9291 capsule.	
Reporting group title	Dose expansion
Reporting group description:	
Pre-treated EGFR T790M mutation positive (by central testing) patient cohort. Dose groups were expanded to include more patients.	
Reporting group title	First line
Reporting group description:	
Cohort of patients receiving first-line treatment for EGFRm advanced NSCLC, in 80mg and 160mg AZD9291 capsule.	
Reporting group title	80mg tablet
Reporting group description:	
US-only cohort of pre-treated EGFR patients receiving the tablet formulation of AZD9291 (80 mg).	
Reporting group title	Japan cytology
Reporting group description:	
Japan-only cohort of patients (EGFR T790M mutation status determined from cytology samples) receiving AZD9291 80 mg tablet.	

Primary: Objective Response Rate (ORR) for dose expansion population

End point title	Objective Response Rate (ORR) for dose expansion
End point description:	
Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. ORR is the percentage of patients with at least 1 visit response of CR or PR (by investigator assessment) that was confirmed at least 4 weeks later, prior to progression or further anti-cancer therapy.	
End point type	Primary
End point timeframe:	
RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 21 months (at time of analysis)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	Dose expansion			
Subject group type	Reporting group			
Number of subjects analysed	175[3]			
Units: % of participants				
number (confidence interval 95%)	64.0 (56.4 to 71.1)			

Notes:

[3] - Patients who are T790m+ve

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) for extension population

End point title	Objective Response Rate (ORR) for extension population[4][5]

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. ORR is the percentage of patients with at least 1 visit response of CR or PR (by independent central review) that was confirmed at least 4 weeks later, prior to progression or further anti-cancer therapy.

End point type	Primary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 12 months (at the time of analysis)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	AZD9291 80mg Extension			
Subject group type	Reporting group			
Number of subjects analysed	198[6]			
Units: % of participants				
number (confidence interval 95%)	61.1 (53.9 to 67.9)			

Notes:

[6] - Some patients do not have baseline measurable lesions

Statistical analyses

No statistical analyses for this end point

Primary: Best Objective Response (BOR) for dose escalation population

End point title	Best Objective Response (BOR) for dose escalation

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response

(PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions; Stable disease (SD): Neither sufficient shrinkage to qualify as a response nor sufficient growth to qualify as progression; Progressive Disease (PD): >= 20% increase in the sum of diameters of TLs and an absolute increase in sum of diameters of >=5mm (compared to the previous minimum sum) or progression of NTLs or a new lesion. Not evaluable (NE): TL response is missing and there is no evidence of progression of NTLs and no new lesions. BOR is the best response (by investigator assessment) a patient has achieved where the order of best to worst is CR, PR, SD, PD, NE prior to or at progression and prior to further anti-cancer therapy.

End point type	Primary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 25 months (at time of analysis)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	Dose escalation			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Number of participants				
Partial Response|	19			
Stable disease|	5			
Progressive disease|	5			
Not evaluable|	2			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) for 1st line population

End point title	Objective Response Rate (ORR) for 1st line population[9][10]

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. ORR is the percentage of patients with at least 1 visit response of CR or PR (by investigator assessment) that was confirmed at least 4 weeks later, prior to progression or further anti-cancer therapy.

End point type	Primary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 21 months (at time of analysis)

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: No statistical hypothesis to be tested. Descriptive statistics are produced.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	First line			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: % of participants				
number (confidence interval 95%)	76.7 (64.0 to 86.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) for dose expansion population

End point title	Duration of Response (DoR) for dose expansion population[11]

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. DoR was defined as the time from the date of first documented response (CR or PR that was subsequently confirmed) until the date of documented progression (PD) or death in the absence of disease progression (by investigator assessment).

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 21 months (at time of analysis)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	Dose expansion			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: months				
median (confidence interval 95%)	9.7 (8.4 to 13.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) for dose expansion population

End point title	Progression-Free Survival (PFS) for dose expansion

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Progressive Disease (PD): >= 20% increase in the sum of diameters of TLs and an absolute increase in sum of diameters of >=5mm (compared to the previous minimum sum) or progression of NTLs or a new lesion. PFS is the time from date of first dose until the date of PD (by independent central review) or death (by any cause in the absence of progression) regardless of whether the patient withdrew from AZD9291

therapy or received another anti-cancer therapy prior to progression. Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST 1.1 assessment.

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 21 months (at time of analysis)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	Dose expansion			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: months				
median (confidence interval 95%)	9.6 (8.3 to 11.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) for 1st line population

End point title	Duration of Response (DoR) for 1st line population[13]

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Progressive Disease (PD): >= 20% increase in the sum of diameters of TLs and an absolute increase in sum of diameters of >=5mm (compared to the previous minimum sum) or progression of NTLs or a new lesion. PFS is the time from date of first dose until the date of PD (by independent central review) or death (by any cause in the absence of progression) regardless of whether the patient withdrew from AZD9291 therapy or received another anti-cancer therapy prior to progression. Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST 1.1 assessment.

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 21 months (at time of analysis)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	First line			
Subject group type	Reporting group			
Number of subjects analysed	46[14]			
Units: months				
median (confidence interval 95%)	18.0 (12.5 to 24.7)			

Notes:

[14] - 46 patients responded as per RECIST v 1.1

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) for 80mg AZD9291 extension population

End point title	Overall Survival (OS) for 80mg AZD9291 extension

End point description:

OS is the time from date of first dose until the date of death (by any cause). Patients who had not died at the time of analysis were censored at the time they were last known to be alive.

End point type	Secondary

End point timeframe:

From randomisation until death, up to approximately 21 months (at time of analysis)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	AZD9291 80mg Extension			
Subject group type	Reporting group			
Number of subjects analysed	201			
Units: months				
median (confidence interval 95%)	24.3 (21.2 to 28.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) for 1st line population

End point title	Progression-Free Survival (PFS) for 1st line population[16]

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Progressive Disease (PD): >= 20% increase in the sum of diameters of TLs and an absolute increase in sum of diameters of >=5mm (compared to the previous minimum sum) or progression of NTLs or a new lesion. PFS is the time from date of first dose until the date of PD (by independent central review) or death (by any cause in the absence of progression) regardless of whether the patient withdrew from AZD9291 therapy or received another anti-cancer therapy prior to progression. Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST 1.1 assessment.

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from randomisation until objective disease progression, up to approximately 21 months (at time of analysis)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical hypothesis to be tested. Descriptive statistics are produced.

End point values	First line			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: months				
median (confidence interval 95%)	20.5 (13.7 to 26.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs from start of study drug until 28 days post treatment discontinuation, up to DCO	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1, 21.0

Reporting groups	
Reporting group title	AZD9291 80mg
Reporting group description: Description (Arm-group)	
Reporting group title	Dose escalation
Reporting group description: Description (Arm-group)	
Reporting group title	Japan cytology
Reporting group description: Description (Arm-group)	
Reporting group title	First Line
Reporting group description: Description (Arm-group)	
Reporting group title	80mg Tablet
Reporting group description: Description (Arm-group)	
Reporting group title	Dose expansion
Reporting group description: Description (Arm-group)	

Serious adverse events	AZD9291 80mg	Dose escalation	Japan cytology
Total subjects affected by serious adverse events			
subjects affected / exposed	85 / 201 (42.29%)	12 / 31 (38.71%)	5 / 28 (17.86%)
number of deaths (all causes)	135	5	2
number of deaths resulting from adverse events	11	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Lymphoma			

subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Follicular thyroid cancer			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer stage i			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large b-cell lymphoma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 central nervous system			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 intramural haematoma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Peripheral artery thrombosis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			
Asthenia			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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

Death			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Fatigue			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (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
Oedema peripheral			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
General physical health deterioration			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (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
Localised oedema			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Malaise			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Pyrexia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Pleural effusion			
subjects affected / exposed	3 / 201 (1.49%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Dyspnoea			

subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Asthma			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Pneumonitis			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	3 / 3	0 / 0	2 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Pneumothorax spontaneous			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Pulmonary artery thrombosis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	5 / 201 (2.49%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary granuloma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 hypertension			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Insomnia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			
Amylase increased			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Alanine aminotransferase increased			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (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
Platelet count decreased			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Lipase increased			

subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Haemoglobin decreased			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 bilirubin increased			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (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
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Fall			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (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
Subdural haematoma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 fracture			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Road traffic accident			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Post procedural complication			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			
Stress cardiomyopathy			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 acute			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 cyst			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 haemorrhage			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral infarction			

subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Cognitive disorder			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Cerebrovascular accident			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebrospinal fluid retention			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Embolic stroke			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Hemiparesis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 nerve disorder			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Intracranial haematoma			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (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
Ischaemic stroke			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoplegia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 disorder			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aplastic anaemia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Microcytic anaemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Febrile neutropenia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Thrombocytopenia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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			
Vertigo			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Corneal erosion			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Abdominal pain upper			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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

Diarrhoea			
subjects affected / exposed	2 / 201 (1.00%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Colitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Gastritis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 obstruction			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Inguinal hernia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (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
Pancreatitis			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (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
Rectal haemorrhage			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 intestine ulcer			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			
Cholangitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 function abnormal			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin toxicity			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous emphysema			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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			

Renal impairment			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 failure			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Hydronephrosis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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			
Back pain			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 column stenosis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pathological fracture			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Pain in extremity			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 chest pain			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 pneumonia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (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
Pyelonephritis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.50%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viraemia			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 infection			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Bacteraemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Device related infection			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (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
Pneumonia viral			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	9 / 201 (4.48%)	4 / 31 (12.90%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 11	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 infection			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (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
Post procedural infection			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 201 (0.00%)	1 / 31 (3.23%)	0 / 28 (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 tract infection			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella sepsis			

subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 tract infection bacterial			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 bacteraemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subperiosteal abscess			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 bacterial			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Viral infection			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 201 (0.50%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (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
Hypoglycaemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
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	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	First Line	80mg Tablet	Dose expansion
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 60 (45.00%)	5 / 12 (41.67%)	103 / 271 (38.01%)
number of deaths (all causes)	5	4	54
number of deaths resulting from adverse events	1	2	13
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lymphoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Follicular thyroid cancer			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer stage i			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Diffuse large b-cell lymphoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Cancer pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 central nervous system			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 intramural haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 physical health deterioration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (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
Dyspnoea			

subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Asthma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	2 / 3	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 artery thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	4 / 60 (6.67%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences causally related to treatment / all	0 / 5	0 / 0	3 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary granuloma			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Pulmonary hypertension			

subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Respiratory failure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
Delirium			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Anxiety			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Insomnia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 bilirubin increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
Limb injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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	2 / 60 (3.33%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	0 / 271 (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
Spinal fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Stress cardiomyopathy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 acute			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Cerebral cyst			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 ischaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid retention			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial nerve disorder			

subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Epilepsy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoplegia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			

subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Syncope			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aplastic anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microcytic anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Pancytopenia			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
Vertigo			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
Corneal erosion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	0 / 271 (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
Constipation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences causally related to treatment / all	1 / 3	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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 obstruction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Intestinal obstruction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 ulcer			

subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Oesophagitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 function abnormal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
Skin toxicity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous emphysema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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			

Renal impairment			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 failure			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 kidney injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Spinal column stenosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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

Pathological fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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	0 / 60 (0.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viraemia			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	0 / 271 (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
Klebsiella infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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 viral			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Mediastinitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	5 / 60 (8.33%)	0 / 12 (0.00%)	13 / 271 (4.80%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 6
Pneumonia pneumococcal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Post procedural infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Rhinovirus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Salmonella sepsis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	1 / 60 (1.67%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Streptococcal bacteraemia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (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
Subperiosteal abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 tract infection bacterial			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	0 / 271 (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
Hypokalaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	AZD9291 80mg	Dose escalation	Japan cytology
Total subjects affected by non-serious adverse events			
subjects affected / exposed	199 / 201 (99.00%)	31 / 31 (100.00%)	26 / 28 (92.86%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	1 / 201 (0.50%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	1	3	0

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	4 / 201 (1.99%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	4	1	0
Hypertension			
subjects affected / exposed	10 / 201 (4.98%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	10	1	0
Thrombosis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	5 / 201 (2.49%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	6	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	32 / 201 (15.92%)	7 / 31 (22.58%)	3 / 28 (10.71%)
occurrences (all)	39	9	3
Malaise			
subjects affected / exposed	5 / 201 (2.49%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	5	0	3
Mucosal inflammation			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Asthenia			
subjects affected / exposed	24 / 201 (11.94%)	3 / 31 (9.68%)	0 / 28 (0.00%)
occurrences (all)	59	3	0
Early satiety			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	2 / 201 (1.00%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	2	2	1
Facial pain			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			

subjects affected / exposed	7 / 201 (3.48%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	12	0	0
Local swelling			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	6 / 201 (2.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	8	0	0
Peripheral swelling			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	20 / 201 (9.95%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences (all)	25	1	2
Oedema peripheral			
subjects affected / exposed	20 / 201 (9.95%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	23	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	6 / 201 (2.99%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	6	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	32 / 201 (15.92%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	35	3	1
Dysphonia			
subjects affected / exposed	4 / 201 (1.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	4	0	0
Cough			
subjects affected / exposed	51 / 201 (25.37%)	4 / 31 (12.90%)	1 / 28 (3.57%)
occurrences (all)	62	4	1
Aspiration			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Epistaxis			

subjects affected / exposed	12 / 201 (5.97%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	14	1	0
Rhinorrhoea			
subjects affected / exposed	7 / 201 (3.48%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	8	3	0
Haemoptysis			
subjects affected / exposed	10 / 201 (4.98%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	12	0	0
Hypoxia			
subjects affected / exposed	4 / 201 (1.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	4	0	0
Nasal discomfort			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nasal inflammation			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	9 / 201 (4.48%)	4 / 31 (12.90%)	0 / 28 (0.00%)
occurrences (all)	9	4	0
Paranasal sinus discomfort			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Pneumonia aspiration			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Pneumonitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	12 / 201 (5.97%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	15	1	0
Pulmonary embolism			

subjects affected / exposed	8 / 201 (3.98%)	3 / 31 (9.68%)	2 / 28 (7.14%)
occurrences (all)	8	4	2
Rhinitis allergic			
subjects affected / exposed	9 / 201 (4.48%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	9	1	0
Sinus congestion			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	4	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	9 / 201 (4.48%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	9	0	1
Confusional state			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	30 / 201 (14.93%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	35	1	0
Depressed mood			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	18 / 201 (8.96%)	4 / 31 (12.90%)	1 / 28 (3.57%)
occurrences (all)	24	4	1
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 201 (7.96%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	25	2	1
Blood alkaline phosphatase increased			

subjects affected / exposed	9 / 201 (4.48%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	9	0	0
Blood creatinine increased			
subjects affected / exposed	13 / 201 (6.47%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	18	3	1
Computerised tomogram thorax abnormal			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram qt prolonged			
subjects affected / exposed	7 / 201 (3.48%)	0 / 31 (0.00%)	5 / 28 (17.86%)
occurrences (all)	21	0	5
White blood cell count decreased			
subjects affected / exposed	18 / 201 (8.96%)	3 / 31 (9.68%)	6 / 28 (21.43%)
occurrences (all)	30	4	16
Renal function test abnormal			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	33 / 201 (16.42%)	1 / 31 (3.23%)	3 / 28 (10.71%)
occurrences (all)	62	2	8
Neutrophil count decreased			
subjects affected / exposed	15 / 201 (7.46%)	3 / 31 (9.68%)	6 / 28 (21.43%)
occurrences (all)	21	6	27
Lymphocyte count decreased			
subjects affected / exposed	6 / 201 (2.99%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	7	0	23
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	12 / 201 (5.97%)	2 / 31 (6.45%)	3 / 28 (10.71%)
occurrences (all)	14	2	3
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	3	0	1
Muscle strain			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	6 / 201 (2.99%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	6	0	2
Rib fracture			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Traumatic fracture			
subjects affected / exposed	4 / 201 (1.99%)	3 / 31 (9.68%)	0 / 28 (0.00%)
occurrences (all)	4	3	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Pericardial effusion			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Visual field defect			
subjects affected / exposed	1 / 201 (0.50%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	1	2	0
Tremor			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Transient ischaemic attack			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 201 (1.49%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	3	2	0
Paraesthesia			
subjects affected / exposed	4 / 201 (1.99%)	3 / 31 (9.68%)	0 / 28 (0.00%)
occurrences (all)	8	3	0
Headache			
subjects affected / exposed	30 / 201 (14.93%)	6 / 31 (19.35%)	1 / 28 (3.57%)
occurrences (all)	35	9	1
Dysgeusia			
subjects affected / exposed	5 / 201 (2.49%)	3 / 31 (9.68%)	2 / 28 (7.14%)
occurrences (all)	5	3	2
Dysarthria			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	16 / 201 (7.96%)	3 / 31 (9.68%)	0 / 28 (0.00%)
occurrences (all)	18	3	0
Carotid artery aneurysm			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	34 / 201 (16.92%)	7 / 31 (22.58%)	6 / 28 (21.43%)
occurrences (all)	42	8	16
Leukopenia			
subjects affected / exposed	10 / 201 (4.98%)	1 / 31 (3.23%)	4 / 28 (14.29%)
occurrences (all)	14	1	12
Lymphadenopathy			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	7 / 201 (3.48%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences (all)	11	1	3

Thrombocytopenia			
subjects affected / exposed	16 / 201 (7.96%)	2 / 31 (6.45%)	2 / 28 (7.14%)
occurrences (all)	19	2	3
Neutropenia			
subjects affected / exposed	14 / 201 (6.97%)	4 / 31 (12.90%)	5 / 28 (17.86%)
occurrences (all)	22	8	14
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Hypoacusis			
subjects affected / exposed	3 / 201 (1.49%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	3	2	0
Vertigo			
subjects affected / exposed	4 / 201 (1.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	5	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	2 / 201 (1.00%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	2	2	0
Cataract			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	5	0	0
Conjunctival haemorrhage			
subjects affected / exposed	3 / 201 (1.49%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	4	2	0
Dry eye			
subjects affected / exposed	14 / 201 (6.97%)	4 / 31 (12.90%)	1 / 28 (3.57%)
occurrences (all)	32	8	2
Eye discharge			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Visual acuity reduced			
subjects affected / exposed	2 / 201 (1.00%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	2	1	0
Eyelid oedema			

subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Macular degeneration			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	6 / 201 (2.99%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	6	3	0
Eye disorder			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	6 / 201 (2.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	7	0	0
Vitreous detachment			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Vitreous floaters			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	35 / 201 (17.41%)	8 / 31 (25.81%)	4 / 28 (14.29%)
occurrences (all)	51	11	5
Anal incontinence			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	7 / 201 (3.48%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	7	1	0

Abdominal distension			
subjects affected / exposed	6 / 201 (2.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	6	0	0
Abdominal pain			
subjects affected / exposed	15 / 201 (7.46%)	3 / 31 (9.68%)	0 / 28 (0.00%)
occurrences (all)	16	3	0
Dyschezia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Chapped lips			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	1 / 201 (0.50%)	1 / 31 (3.23%)	3 / 28 (10.71%)
occurrences (all)	1	1	3
Constipation			
subjects affected / exposed	52 / 201 (25.87%)	3 / 31 (9.68%)	5 / 28 (17.86%)
occurrences (all)	60	4	5
Diarrhoea			
subjects affected / exposed	103 / 201 (51.24%)	19 / 31 (61.29%)	10 / 28 (35.71%)
occurrences (all)	270	44	14
Dry mouth			
subjects affected / exposed	14 / 201 (6.97%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	14	1	1
Abdominal pain upper			
subjects affected / exposed	16 / 201 (7.96%)	3 / 31 (9.68%)	1 / 28 (3.57%)
occurrences (all)	27	4	1
Dyspepsia			
subjects affected / exposed	15 / 201 (7.46%)	4 / 31 (12.90%)	0 / 28 (0.00%)
occurrences (all)	15	4	0
Dysphagia			
subjects affected / exposed	6 / 201 (2.99%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	8	3	0
Flatulence			
subjects affected / exposed	3 / 201 (1.49%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	3	2	0

Gastritis			
subjects affected / exposed	4 / 201 (1.99%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	5	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	8 / 201 (3.98%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	8	1	0
Haemorrhoids			
subjects affected / exposed	5 / 201 (2.49%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	5	1	0
Mouth ulceration			
subjects affected / exposed	5 / 201 (2.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	5	0	0
Nausea			
subjects affected / exposed	54 / 201 (26.87%)	10 / 31 (32.26%)	5 / 28 (17.86%)
occurrences (all)	77	11	5
Oesophageal stenosis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	35 / 201 (17.41%)	8 / 31 (25.81%)	10 / 28 (35.71%)
occurrences (all)	45	14	15
Toothache			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Lip pain			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Onychoclasis			
subjects affected / exposed	13 / 201 (6.47%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	13	1	1
Nail disorder			
subjects affected / exposed	6 / 201 (2.99%)	3 / 31 (9.68%)	3 / 28 (10.71%)
occurrences (all)	8	3	3
Nail discolouration			

subjects affected / exposed	5 / 201 (2.49%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	6	2	0
Erythema			
subjects affected / exposed	9 / 201 (4.48%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences (all)	9	1	2
Eczema			
subjects affected / exposed	3 / 201 (1.49%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences (all)	3	2	2
Ecchymosis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	53 / 201 (26.37%)	9 / 31 (29.03%)	12 / 28 (42.86%)
occurrences (all)	57	9	12
Dermatitis acneiform			
subjects affected / exposed	17 / 201 (8.46%)	3 / 31 (9.68%)	2 / 28 (7.14%)
occurrences (all)	22	3	2
Alopecia			
subjects affected / exposed	8 / 201 (3.98%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences (all)	10	1	2
Acne			
subjects affected / exposed	4 / 201 (1.99%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	10	0	1
Palmar erythema			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin sensitisation			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Skin irritation			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	13 / 201 (6.47%)	4 / 31 (12.90%)	1 / 28 (3.57%)
occurrences (all)	14	6	2
Skin exfoliation			

subjects affected / exposed	2 / 201 (1.00%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	2	2	1
Rash papular			
subjects affected / exposed	4 / 201 (1.99%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	4	0	2
Rash macular			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Rash erythematous			
subjects affected / exposed	1 / 201 (0.50%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	1	2	1
Rash			
subjects affected / exposed	53 / 201 (26.37%)	10 / 31 (32.26%)	4 / 28 (14.29%)
occurrences (all)	66	16	4
Pruritus			
subjects affected / exposed	36 / 201 (17.91%)	8 / 31 (25.81%)	4 / 28 (14.29%)
occurrences (all)	49	10	4
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	11 / 201 (5.47%)	3 / 31 (9.68%)	1 / 28 (3.57%)
occurrences (all)	17	6	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Nocturia			

subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	13 / 201 (6.47%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	13	1	0
Myalgia			
subjects affected / exposed	15 / 201 (7.46%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	15	2	1
Musculoskeletal pain			
subjects affected / exposed	26 / 201 (12.94%)	2 / 31 (6.45%)	2 / 28 (7.14%)
occurrences (all)	30	2	2
Musculoskeletal chest pain			
subjects affected / exposed	14 / 201 (6.97%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	16	0	0
Muscular weakness			
subjects affected / exposed	5 / 201 (2.49%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	5	2	2
Muscle spasms			
subjects affected / exposed	19 / 201 (9.45%)	3 / 31 (9.68%)	1 / 28 (3.57%)
occurrences (all)	23	4	1
Muscle atrophy			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	41 / 201 (20.40%)	5 / 31 (16.13%)	3 / 28 (10.71%)
occurrences (all)	52	8	3
Arthritis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	24 / 201 (11.94%)	4 / 31 (12.90%)	3 / 28 (10.71%)
occurrences (all)	30	4	3
Pain in extremity			

subjects affected / exposed	15 / 201 (7.46%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	16	0	0
Infections and infestations			
Oral herpes			
subjects affected / exposed	3 / 201 (1.49%)	2 / 31 (6.45%)	2 / 28 (7.14%)
occurrences (all)	3	2	2
Cystitis			
subjects affected / exposed	10 / 201 (4.98%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	12	1	1
Abscess limb			
subjects affected / exposed	1 / 201 (0.50%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	9 / 201 (4.48%)	2 / 31 (6.45%)	1 / 28 (3.57%)
occurrences (all)	10	2	1
Conjunctivitis			
subjects affected / exposed	11 / 201 (5.47%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences (all)	20	2	2
Folliculitis			
subjects affected / exposed	3 / 201 (1.49%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	3	2	0
Gastroenteritis			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	4	0	2
Lower respiratory tract infection			
subjects affected / exposed	2 / 201 (1.00%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	2	7	0
Lung infection			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Lymphangitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	18 / 201 (8.96%)	7 / 31 (22.58%)	3 / 28 (10.71%)
occurrences (all)	24	11	3

Sinusitis			
subjects affected / exposed	7 / 201 (3.48%)	2 / 31 (6.45%)	0 / 28 (0.00%)
occurrences (all)	7	2	0
Pharyngitis			
subjects affected / exposed	9 / 201 (4.48%)	0 / 31 (0.00%)	3 / 28 (10.71%)
occurrences (all)	10	0	4
Pneumonia			
subjects affected / exposed	9 / 201 (4.48%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	11	1	1
Pneumonia bacterial			
subjects affected / exposed	2 / 201 (1.00%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	2	0	2
Rash pustular			
subjects affected / exposed	5 / 201 (2.49%)	1 / 31 (3.23%)	0 / 28 (0.00%)
occurrences (all)	9	4	0
Rhinitis			
subjects affected / exposed	3 / 201 (1.49%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Paronychia			
subjects affected / exposed	56 / 201 (27.86%)	8 / 31 (25.81%)	11 / 28 (39.29%)
occurrences (all)	74	11	12
Upper respiratory tract infection			
subjects affected / exposed	31 / 201 (15.42%)	7 / 31 (22.58%)	5 / 28 (17.86%)
occurrences (all)	45	19	7
Urinary tract infection			
subjects affected / exposed	18 / 201 (8.96%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	25	1	1
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	5 / 201 (2.49%)	0 / 31 (0.00%)	2 / 28 (7.14%)
occurrences (all)	6	0	2
Hyperkalaemia			
subjects affected / exposed	5 / 201 (2.49%)	1 / 31 (3.23%)	3 / 28 (10.71%)
occurrences (all)	8	1	3
Hyperglycaemia			

subjects affected / exposed	6 / 201 (2.99%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	8	0	0
Dehydration			
subjects affected / exposed	4 / 201 (1.99%)	2 / 31 (6.45%)	2 / 28 (7.14%)
occurrences (all)	6	3	2
Decreased appetite			
subjects affected / exposed	51 / 201 (25.37%)	12 / 31 (38.71%)	5 / 28 (17.86%)
occurrences (all)	60	18	6
Hypocalcaemia			
subjects affected / exposed	7 / 201 (3.48%)	3 / 31 (9.68%)	0 / 28 (0.00%)
occurrences (all)	9	3	0
Hyponatraemia			
subjects affected / exposed	10 / 201 (4.98%)	0 / 31 (0.00%)	0 / 28 (0.00%)
occurrences (all)	10	0	0
Hypokalaemia			
subjects affected / exposed	10 / 201 (4.98%)	1 / 31 (3.23%)	1 / 28 (3.57%)
occurrences (all)	12	2	1

Non-serious adverse events	First Line	80mg Tablet	Dose expansion
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 60 (100.00%)	12 / 12 (100.00%)	267 / 271 (98.52%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	10 / 271 (3.69%)
occurrences (all)	2	1	12
Hypertension			
subjects affected / exposed	4 / 60 (6.67%)	2 / 12 (16.67%)	10 / 271 (3.69%)
occurrences (all)	6	2	11
Thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Hypotension			

subjects affected / exposed	2 / 60 (3.33%)	2 / 12 (16.67%)	4 / 271 (1.48%)
occurrences (all)	2	2	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	20 / 60 (33.33%)	2 / 12 (16.67%)	69 / 271 (25.46%)
occurrences (all)	23	4	81
Malaise			
subjects affected / exposed	5 / 60 (8.33%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	5	0	4
Mucosal inflammation			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences (all)	4	0	14
Asthenia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	30 / 271 (11.07%)
occurrences (all)	2	1	43
Early satiety			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	2	0	3
Facial pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Influenza like illness			
subjects affected / exposed	9 / 60 (15.00%)	0 / 12 (0.00%)	11 / 271 (4.06%)
occurrences (all)	12	0	16
Local swelling			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	0	1	3
Non-cardiac chest pain			
subjects affected / exposed	2 / 60 (3.33%)	2 / 12 (16.67%)	4 / 271 (1.48%)
occurrences (all)	2	3	4
Peripheral swelling			

subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	0	1	4
Pyrexia			
subjects affected / exposed	12 / 60 (20.00%)	2 / 12 (16.67%)	32 / 271 (11.81%)
occurrences (all)	13	2	35
Oedema peripheral			
subjects affected / exposed	5 / 60 (8.33%)	2 / 12 (16.67%)	27 / 271 (9.96%)
occurrences (all)	7	4	29
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	5 / 271 (1.85%)
occurrences (all)	1	1	5
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	7 / 60 (11.67%)	5 / 12 (41.67%)	49 / 271 (18.08%)
occurrences (all)	10	6	59
Dysphonia			
subjects affected / exposed	0 / 60 (0.00%)	2 / 12 (16.67%)	13 / 271 (4.80%)
occurrences (all)	0	2	13
Cough			
subjects affected / exposed	17 / 60 (28.33%)	3 / 12 (25.00%)	71 / 271 (26.20%)
occurrences (all)	25	3	87
Aspiration			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Epistaxis			
subjects affected / exposed	9 / 60 (15.00%)	1 / 12 (8.33%)	15 / 271 (5.54%)
occurrences (all)	11	2	17
Rhinorrhoea			
subjects affected / exposed	7 / 60 (11.67%)	2 / 12 (16.67%)	24 / 271 (8.86%)
occurrences (all)	8	2	26
Haemoptysis			
subjects affected / exposed	5 / 60 (8.33%)	1 / 12 (8.33%)	8 / 271 (2.95%)
occurrences (all)	5	2	8
Hypoxia			

subjects affected / exposed	1 / 60 (1.67%)	3 / 12 (25.00%)	1 / 271 (0.37%)
occurrences (all)	1	5	1
Nasal discomfort			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Nasal inflammation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	0	1	4
Oropharyngeal pain			
subjects affected / exposed	4 / 60 (6.67%)	3 / 12 (25.00%)	12 / 271 (4.43%)
occurrences (all)	5	4	13
Paranasal sinus discomfort			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	4 / 271 (1.48%)
occurrences (all)	1	1	5
Pneumonia aspiration			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Pneumonitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	1	1	3
Productive cough			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	12 / 271 (4.43%)
occurrences (all)	0	1	13
Pulmonary embolism			
subjects affected / exposed	3 / 60 (5.00%)	2 / 12 (16.67%)	11 / 271 (4.06%)
occurrences (all)	3	2	11
Rhinitis allergic			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	6 / 271 (2.21%)
occurrences (all)	2	1	6
Sinus congestion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Sneezing			

subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Wheezing			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	5 / 271 (1.85%)
occurrences (all)	0	1	5
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 60 (6.67%)	2 / 12 (16.67%)	13 / 271 (4.80%)
occurrences (all)	4	2	14
Confusional state			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	12 / 60 (20.00%)	3 / 12 (25.00%)	30 / 271 (11.07%)
occurrences (all)	16	3	32
Depressed mood			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	5 / 271 (1.85%)
occurrences (all)	0	1	6
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 60 (11.67%)	0 / 12 (0.00%)	18 / 271 (6.64%)
occurrences (all)	10	0	27
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	21 / 271 (7.75%)
occurrences (all)	11	0	31
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	15 / 271 (5.54%)
occurrences (all)	3	0	15
Blood creatinine increased			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	13 / 271 (4.80%)
occurrences (all)	4	0	19
Computerised tomogram thorax abnormal			
subjects affected / exposed	1 / 60 (1.67%)	3 / 12 (25.00%)	0 / 271 (0.00%)
occurrences (all)	1	3	0
Electrocardiogram qt prolonged			

subjects affected / exposed	5 / 60 (8.33%)	1 / 12 (8.33%)	10 / 271 (3.69%)
occurrences (all)	5	1	11
White blood cell count decreased			
subjects affected / exposed	12 / 60 (20.00%)	0 / 12 (0.00%)	11 / 271 (4.06%)
occurrences (all)	25	0	25
Renal function test abnormal			
subjects affected / exposed	0 / 60 (0.00%)	2 / 12 (16.67%)	0 / 271 (0.00%)
occurrences (all)	0	2	0
Platelet count decreased			
subjects affected / exposed	13 / 60 (21.67%)	0 / 12 (0.00%)	26 / 271 (9.59%)
occurrences (all)	18	0	39
Neutrophil count decreased			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	19 / 271 (7.01%)
occurrences (all)	9	0	47
Lymphocyte count decreased			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	3	0	8
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	14 / 60 (23.33%)	1 / 12 (8.33%)	26 / 271 (9.59%)
occurrences (all)	15	1	26
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	4 / 271 (1.48%)
occurrences (all)	0	1	5
Muscle strain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Procedural pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
Rib fracture			

subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Traumatic fracture			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	2	0	5
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 60 (5.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	3	1	2
Pericardial effusion			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Supraventricular tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	0	1	2
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	4 / 271 (1.48%)
occurrences (all)	1	1	5
Visual field defect			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	1	2	2
Transient ischaemic attack			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	8 / 271 (2.95%)
occurrences (all)	6	0	11
Paraesthesia			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	4	0	10
Headache			

subjects affected / exposed	9 / 60 (15.00%)	1 / 12 (8.33%)	40 / 271 (14.76%)
occurrences (all)	14	6	50
Dysgeusia			
subjects affected / exposed	10 / 60 (16.67%)	1 / 12 (8.33%)	15 / 271 (5.54%)
occurrences (all)	12	1	17
Dysarthria			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	1	1	3
Dizziness			
subjects affected / exposed	9 / 60 (15.00%)	2 / 12 (16.67%)	27 / 271 (9.96%)
occurrences (all)	9	3	34
Carotid artery aneurysm			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 60 (26.67%)	1 / 12 (8.33%)	41 / 271 (15.13%)
occurrences (all)	18	1	60
Leukopenia			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	10 / 271 (3.69%)
occurrences (all)	7	0	22
Lymphadenopathy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Lymphopenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	1	0	9
Thrombocytopenia			
subjects affected / exposed	7 / 60 (11.67%)	2 / 12 (16.67%)	23 / 271 (8.49%)
occurrences (all)	12	2	34
Neutropenia			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	15 / 271 (5.54%)
occurrences (all)	14	0	18
Ear and labyrinth disorders			
Tinnitus			

subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	4 / 271 (1.48%)
occurrences (all)	1	1	4
Hypoacusis			
subjects affected / exposed	1 / 60 (1.67%)	2 / 12 (16.67%)	8 / 271 (2.95%)
occurrences (all)	1	2	8
Vertigo			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	2	1	4
Eye disorders			
Blepharitis			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	4	0	6
Cataract			
subjects affected / exposed	3 / 60 (5.00%)	1 / 12 (8.33%)	6 / 271 (2.21%)
occurrences (all)	3	1	7
Conjunctival haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	1	0	6
Dry eye			
subjects affected / exposed	7 / 60 (11.67%)	1 / 12 (8.33%)	20 / 271 (7.38%)
occurrences (all)	14	2	42
Eye discharge			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	2	0	1
Visual acuity reduced			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	1	1	3
Eyelid oedema			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	1	1	2
Lacrimation increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	0	1	3
Macular degeneration			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0

Photopsia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	1	2	1
Vision blurred			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	1	0	5
Eye disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	3 / 60 (5.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	3	2	2
Vitreous detachment			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	4 / 271 (1.48%)
occurrences (all)	1	1	5
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	14 / 60 (23.33%)	1 / 12 (8.33%)	53 / 271 (19.56%)
occurrences (all)	19	1	92
Anal incontinence			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	5 / 271 (1.85%)
occurrences (all)	1	2	5
Abdominal distension			
subjects affected / exposed	4 / 60 (6.67%)	2 / 12 (16.67%)	13 / 271 (4.80%)
occurrences (all)	6	3	16
Abdominal pain			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	30 / 271 (11.07%)
occurrences (all)	4	0	33
Dyschezia			

subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Chapped lips			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	2	0
Cheilitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	2	0	4
Constipation			
subjects affected / exposed	25 / 60 (41.67%)	2 / 12 (16.67%)	70 / 271 (25.83%)
occurrences (all)	28	2	83
Diarrhoea			
subjects affected / exposed	43 / 60 (71.67%)	5 / 12 (41.67%)	152 / 271 (56.09%)
occurrences (all)	82	7	259
Dry mouth			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	17 / 271 (6.27%)
occurrences (all)	6	0	18
Abdominal pain upper			
subjects affected / exposed	13 / 60 (21.67%)	0 / 12 (0.00%)	21 / 271 (7.75%)
occurrences (all)	17	0	29
Dyspepsia			
subjects affected / exposed	6 / 60 (10.00%)	1 / 12 (8.33%)	19 / 271 (7.01%)
occurrences (all)	6	1	22
Dysphagia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	11 / 271 (4.06%)
occurrences (all)	2	1	11
Flatulence			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	6 / 271 (2.21%)
occurrences (all)	0	1	6
Gastritis			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	6	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	8 / 60 (13.33%)	2 / 12 (16.67%)	11 / 271 (4.06%)
occurrences (all)	9	2	12
Haemorrhoids			

subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	7	0	6
Mouth ulceration			
subjects affected / exposed	8 / 60 (13.33%)	0 / 12 (0.00%)	8 / 271 (2.95%)
occurrences (all)	10	0	8
Nausea			
subjects affected / exposed	17 / 60 (28.33%)	7 / 12 (58.33%)	81 / 271 (29.89%)
occurrences (all)	28	8	113
Oesophageal stenosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	2
Stomatitis			
subjects affected / exposed	30 / 60 (50.00%)	1 / 12 (8.33%)	57 / 271 (21.03%)
occurrences (all)	62	1	79
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	6 / 271 (2.21%)
occurrences (all)	1	2	6
Lip pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Onychoclasis			
subjects affected / exposed	3 / 60 (5.00%)	3 / 12 (25.00%)	7 / 271 (2.58%)
occurrences (all)	3	3	7
Nail disorder			
subjects affected / exposed	3 / 60 (5.00%)	1 / 12 (8.33%)	11 / 271 (4.06%)
occurrences (all)	3	1	12
Nail discolouration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences (all)	3	0	14
Eczema			
subjects affected / exposed	5 / 60 (8.33%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	5	0	4

Ecchymosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	26 / 60 (43.33%)	4 / 12 (33.33%)	64 / 271 (23.62%)
occurrences (all)	34	4	80
Dermatitis acneiform			
subjects affected / exposed	18 / 60 (30.00%)	1 / 12 (8.33%)	41 / 271 (15.13%)
occurrences (all)	20	1	52
Alopecia			
subjects affected / exposed	5 / 60 (8.33%)	2 / 12 (16.67%)	12 / 271 (4.43%)
occurrences (all)	6	2	12
Acne			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences (all)	4	0	13
Palmar erythema			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	2	0
Skin sensitisation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Skin irritation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Skin fissures			
subjects affected / exposed	9 / 60 (15.00%)	1 / 12 (8.33%)	31 / 271 (11.44%)
occurrences (all)	9	1	33
Skin exfoliation			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	15 / 271 (5.54%)
occurrences (all)	3	0	16
Rash papular			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	2	0	4
Rash macular			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	8	0	6

Rash erythematous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	0	0	8
Rash			
subjects affected / exposed	22 / 60 (36.67%)	3 / 12 (25.00%)	76 / 271 (28.04%)
occurrences (all)	27	3	105
Pruritus			
subjects affected / exposed	16 / 60 (26.67%)	3 / 12 (25.00%)	61 / 271 (22.51%)
occurrences (all)	18	4	72
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	6	0	1
Rash maculo-papular			
subjects affected / exposed	7 / 60 (11.67%)	1 / 12 (8.33%)	12 / 271 (4.43%)
occurrences (all)	9	2	22
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	2	1	3
Hydronephrosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
Haematuria			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	6 / 271 (2.21%)
occurrences (all)	0	1	6
Nocturia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	0	1	3
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	8 / 271 (2.95%)
occurrences (all)	1	0	8
Myalgia			
subjects affected / exposed	4 / 60 (6.67%)	3 / 12 (25.00%)	17 / 271 (6.27%)
occurrences (all)	4	4	18
Musculoskeletal pain			

subjects affected / exposed	5 / 60 (8.33%)	2 / 12 (16.67%)	25 / 271 (9.23%)
occurrences (all)	5	2	26
Musculoskeletal chest pain			
subjects affected / exposed	8 / 60 (13.33%)	3 / 12 (25.00%)	22 / 271 (8.12%)
occurrences (all)	10	4	23
Muscular weakness			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	3	0	6
Muscle spasms			
subjects affected / exposed	8 / 60 (13.33%)	2 / 12 (16.67%)	32 / 271 (11.81%)
occurrences (all)	10	5	38
Muscle atrophy			
subjects affected / exposed	0 / 60 (0.00%)	2 / 12 (16.67%)	1 / 271 (0.37%)
occurrences (all)	0	2	1
Back pain			
subjects affected / exposed	9 / 60 (15.00%)	2 / 12 (16.67%)	38 / 271 (14.02%)
occurrences (all)	11	2	43
Arthritis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	2	1	3
Arthralgia			
subjects affected / exposed	6 / 60 (10.00%)	2 / 12 (16.67%)	30 / 271 (11.07%)
occurrences (all)	7	2	46
Pain in extremity			
subjects affected / exposed	5 / 60 (8.33%)	4 / 12 (33.33%)	30 / 271 (11.07%)
occurrences (all)	8	7	37
Infections and infestations			
Oral herpes			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	0	1	2
Cystitis			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	5	0	8
Abscess limb			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0

Bronchitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	8 / 271 (2.95%)
occurrences (all)	1	0	10
Conjunctivitis			
subjects affected / exposed	8 / 60 (13.33%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	9	0	6
Folliculitis			
subjects affected / exposed	5 / 60 (8.33%)	0 / 12 (0.00%)	14 / 271 (5.17%)
occurrences (all)	5	0	15
Gastroenteritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	1	0	4
Lower respiratory tract infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	2	0	8
Lung infection			
subjects affected / exposed	2 / 60 (3.33%)	1 / 12 (8.33%)	4 / 271 (1.48%)
occurrences (all)	3	1	4
Lymphangitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	4 / 60 (6.67%)	1 / 12 (8.33%)	25 / 271 (9.23%)
occurrences (all)	6	1	33
Sinusitis			
subjects affected / exposed	3 / 60 (5.00%)	2 / 12 (16.67%)	11 / 271 (4.06%)
occurrences (all)	3	4	15
Pharyngitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 12 (0.00%)	8 / 271 (2.95%)
occurrences (all)	2	0	8
Pneumonia			
subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	11 / 271 (4.06%)
occurrences (all)	6	0	11
Pneumonia bacterial			
subjects affected / exposed	0 / 60 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1

Rash pustular			
subjects affected / exposed	3 / 60 (5.00%)	2 / 12 (16.67%)	4 / 271 (1.48%)
occurrences (all)	4	2	4
Rhinitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	1	1	3
Paronychia			
subjects affected / exposed	28 / 60 (46.67%)	2 / 12 (16.67%)	71 / 271 (26.20%)
occurrences (all)	39	3	92
Upper respiratory tract infection			
subjects affected / exposed	16 / 60 (26.67%)	4 / 12 (33.33%)	33 / 271 (12.18%)
occurrences (all)	29	4	36
Urinary tract infection			
subjects affected / exposed	10 / 60 (16.67%)	2 / 12 (16.67%)	25 / 271 (9.23%)
occurrences (all)	17	3	32
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	3 / 60 (5.00%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences (all)	4	0	14
Hyperkalaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	1	0	12
Hyperglycaemia			
subjects affected / exposed	4 / 60 (6.67%)	1 / 12 (8.33%)	11 / 271 (4.06%)
occurrences (all)	7	1	22
Dehydration			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	9 / 271 (3.32%)
occurrences (all)	2	1	10
Decreased appetite			
subjects affected / exposed	19 / 60 (31.67%)	5 / 12 (41.67%)	79 / 271 (29.15%)
occurrences (all)	20	7	95
Hypocalcaemia			
subjects affected / exposed	4 / 60 (6.67%)	0 / 12 (0.00%)	10 / 271 (3.69%)
occurrences (all)	4	0	14
Hyponatraemia			

subjects affected / exposed	6 / 60 (10.00%)	0 / 12 (0.00%)	17 / 271 (6.27%)
occurrences (all)	8	0	34
Hypokalaemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 12 (8.33%)	10 / 271 (3.69%)
occurrences (all)	1	3	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Data cut on 01MAY2018 for final OS for extension cohort and final PFS, DoR and ORR for 1st line cohort. AEs used MedDRA 21.0. All remaining data/cohorts reported with a data cut of 01NOV2016. AEs used MedDRA 19.1. No comparisons as single arm.

Notes: