Clinical trial results:
International, Multicenter, Open-Label, Treatment-Extension Study for Subjects Who Completed a Phase 1 or Phase 2 Parental Study to Continue Receiving Treatment With SAR245408 or SAR245409 as a Monotherapy or as a Combination Regimen

Summary

EudraCT number	2011-006140-78
Trial protocol	ES FR BE
Global end of trial date	23 May 2018

Results information

Result version number	v1 (current)
This version publication date	06 June 2019
First version publication date	06 June 2019

Trial information

Trial identification

Sponsor protocol code	TED12414

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01587040
WHO universal trial number (UTN)	U1111-1124-1403

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Sanofi aventis recherche & développement, Trial Transparency Team, Contact-US@sanofi.com
Scientific contact	Sanofi aventis recherche & développement, Trial Transparency Team, Contact-US@sanofi.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	13 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the long term safety and tolerability of SAR245408 and SAR245409 (investigational medicinal product [IMP]) as a monotherapy or as part of a combination regimen in subjects who were benefiting from treatment.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	20 July 2012
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	Belgium: 6
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 49
Worldwide total number of subjects	61
EEA total number of subjects	12

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)	36
From 65 to 84 years	24
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 21 centers in 4 countries between 20 July 2012 and 23 May 2018. Subjects who received SAR245408/SAR245409 (IMP) in parental studies (TED12471 [NCT01596270], ARD11437 [NCT01082068], TED12863 [NCT01943838]) were included in study. A total of 67 subjects were screened and 61 subjects were enrolled in this study.

Pre-assignment

Screening details:

Subjects who received IMP for <2 cycles in parental study, and subjects who took a daily dose of IMP higher than their established dose entered treatment-extension study on Day 1 of initiation period; subjects who received IMP >=2 cycles in parental study entered treatment-extension study on Day 1 of extension period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SAR245408: Monotherapy

Arm description:

Subjects received SAR245408 400 milligrams (mg) once daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days).

Arm type	Experimental
Investigational medicinal product name	SAR245408
Investigational medicinal product code	
Other name	XL147
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

SAR245408 was taken with 8 ounces (240 mL) of water, with no food allowed for at least 2 hours before and 1 hour after dosing.

Arm title	SAR245408: Combination Regimen

Arm description:

Subjects received SAR245408 400 mg once daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days). Commercially available drugs were used as combination medications with SAR245408 (depending on the parental study, the following drugs were used in combination with SAR245408: paclitaxel and carboplatin, letrozole, trastuzumab, paclitaxel and trastuzumab).

Arm type	Experimental
Investigational medicinal product name	SAR245408
Investigational medicinal product code	
Other name	XL147
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

SAR245408 was taken with 8 ounces (240 mL) of water, with no food allowed for at least 2 hours before and 1 hour after dosing.

Arm title	SAR245409: Monotherapy

Arm description:

Subjects received SAR245409 50 mg twice daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days).

Arm type	Experimental
Investigational medicinal product name	SAR245409
Investigational medicinal product code	
Other name	XL765
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SAR245409 was taken with 8 ounces (240 mL) of water, with no food allowed for at least 2 hours before and 1 hour after dosing.

Arm title	SAR245409: Combination Regimen

Arm description:

Subjects received SAR245409 50 mg twice daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days). Commercially available drugs were used as combination medications with SAR245409 (depending on the parental study, the following drugs were used in combination with SAR245409: letrozole, temozolomide, rituximab, bendamustine and rituximab).

Arm type	Experimental
Investigational medicinal product name	SAR245409
Investigational medicinal product code	
Other name	XL765
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SAR245409 was taken with 8 ounces (240 mL) of water, with no food allowed for at least 2 hours before and 1 hour after dosing.

Number of subjects in period 1	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy
Started	17	3	37
Completed	0	0	0
Not completed	17	3	37
Disease progression	12	1	15
Adverse event	-	1	10
Other than specified	5	1	11
Protocol deviation	-	-	1

Number of subjects in period 1	SAR245409: Combination Regimen
Started	4
Completed	0
Not completed	4
Disease progression	3
Adverse event	-

Other than specified	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	SAR245408: Monotherapy
Reporting group description:	
Subjects received SAR245408 400 milligrams (mg) once daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days).	
Reporting group title	SAR245408: Combination Regimen
Reporting group description:	
Subjects received SAR245408 400 mg once daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days). Commercially available drugs were used as combination medications with SAR245408 (depending on the parental study, the following drugs were used in combination with SAR245408: paclitaxel and carboplatin, letrozole, trastuzumab, paclitaxel and trastuzumab).	
Reporting group title	SAR245409: Monotherapy
Reporting group description:	
Subjects received SAR245409 50 mg twice daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days).	
Reporting group title	SAR245409: Combination Regimen
Reporting group description:	
Subjects received SAR245409 50 mg twice daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days). Commercially available drugs were used as combination medications with SAR245409 (depending on the parental study, the following drugs were used in combination with SAR245409: letrozole, temozolomide, rituximab, bendamustine and rituximab).	

Reporting group values	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy
Number of subjects	17	3	37
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	61.6	53.7	62.4
standard deviation	± 13.1	± 2.1	± 12.0
Gender categorical Units: Subjects			
Female	12	3	16
Male	5	0	21
Race Units: Subjects			
Caucasian/White	14	2	31
Black	3	0	5
Asian/Oriental	0	1	0
Other	0	0	1
Ethnicity Units: Subjects			

Hispanic	0	1	2
Not hispanic	17	2	35

Reporting group values	SAR245409: Combination Regimen	Total	
Number of subjects	4	61	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	50.0		
standard deviation	± 15.8	-	
Gender categorical Units: Subjects			
Female	0	31	
Male	4	30	
Race Units: Subjects			
Caucasian/White	4	51	
Black	0	8	
Asian/Oriental	0	1	
Other	0	1	
Ethnicity Units: Subjects			
Hispanic	0	3	
Not hispanic	4	58	

End points

End points reporting groups

Reporting group title	SAR245408: Monotherapy

Reporting group description:

Subjects received SAR245408 400 milligrams (mg) once daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days).

Reporting group title	SAR245408: Combination Regimen

Reporting group description:

Subjects received SAR245408 400 mg once daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days). Commercially available drugs were used as combination medications with SAR245408 (depending on the parental study, the following drugs were used in combination with SAR245408: paclitaxel and carboplatin, letrozole, trastuzumab, paclitaxel and trastuzumab).

Reporting group title	SAR245409: Monotherapy

Reporting group description:

Subjects received SAR245409 50 mg twice daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days).

Reporting group title	SAR245409: Combination Regimen

Reporting group description:

Subjects received SAR245409 50 mg twice daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days). Commercially available drugs were used as combination medications with SAR245409 (depending on the parental study, the following drugs were used in combination with SAR245409: letrozole, temozolomide, rituximab, bendamustine and rituximab).

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)[1]

End point description:

Any untoward medical occurrence in a subject who received IMP was considered an AE without regard to possibility of causal relationship with this treatment. Serious adverse event (SAE): any untoward medical occurrence that resulted in any of the following outcomes: death, life-threatening, required initial/prolonged in-patient hospitalization,persistent/significant disability/incapacity, congenital anomaly/birth defect/considered as medically important event. TEAEs: AEs that developed/worsened/became serious during on-treatment period(time from IMP until 30 days after last dose of any IMP). Any TEAE included subjects with both SAE & non-SAEs. TEAE included subjects with any treatment-emergent SAE (TESAE). TEAEs that led to death, dose reduction and/or delay, discontinuation & AEs related to treatment were reported. Grades (3=severe, 4=life-threatening/disabling) represents severity of AEs. Safety population included all subjects who took at least 1 dose of study drug during the study.

End point type	Primary

End point timeframe:

From Baseline up to 30 days after the last dose (maximum exposure: 1959 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy	SAR245409: Combination Regimen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	37	4
Units: subjects				
Any TEAE	16	3	35	3
Any Grade 3-4 TEAEs	12	2	19	1
Any related TEAEs	12	3	23	2
Any Grade 3-4 related TEAE	3	0	11	0
Any Serious TEAE	9	1	10	0
Any Grade 3-4 TESAE	9	1	9	0
Any related TESAE	2	0	1	0
Any Grade 3-4 related TESAE	2	0	0	0
Any TEAE leading to death	0	0	3	0
Any TEAE leading to permanent discontinuation	1	1	8	0
Any TEAE leading to dose reduction	3	1	9	1
Any TEAE leading to dose delay or interruption	6	2	16	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Hematological Parameters

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Hematological Parameters[2]

End point description:

Hematological parameters assessed were anemia, neutropenia and thrombocytopenia. Parameters were assessed as per the National Cancer Institute Common Terminology Criteria for Adverse Experience version 4.03 (NCI-CTCAE v 4.03), where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. Analysis was performed on safety population. Here, "subjects analysed" = subjects with available data for this end point.

End point type	Primary

End point timeframe:

From Baseline up to 30 days after the last dose (maximum exposure: 1959 days)

Notes:

[2] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy	SAR245409: Combination Regimen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	36	4
Units: subjects				
Anemia: All grades	13	1	23	1
Anemia: Grade 1	6	1	18	1
Anemia: Grade 2	3	0	2	0
Anemia: Grade 3	4	0	3	0

Anemia: Grade 4	0	0	0	0
Neutropenia: All grades	7	0	10	1
Neutropenia: Grade 1	2	0	5	1
Neutropenia: Grade 2	2	0	1	0
Neutropenia: Grade 3	2	0	2	0
Neutropenia: Grade 4	1	0	2	0
Thrombocytopenia: All grades	8	0	20	3
Thrombocytopenia: Grade 1	5	0	17	3
Thrombocytopenia: Grade 2	0	0	2	0
Thrombocytopenia: Grade 3	0	0	0	0
Thrombocytopenia: Grade 4	3	0	1	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Biochemical Parameters

End point title	Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Biochemical Parameters[3]

End point description:

Biochemical parameters assessed were hyperglycemia, aspartate aminotransferase (ASAT) increased, alanine aminotransferase (ALAT) increased, hyperbilirubinemia, hypocalcemia, creatinine increased. Parameters were assessed as per the NCI-CTCAE v 4.03, where Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life Threatening. Grade refers to the severity of the AEs. Analysis was performed on safety population. Here, "n"= subjects with available data for specified category.

End point type	Primary

End point timeframe:

From Baseline up to 30 days after the last dose (maximum exposure: 1959 days)

Notes:

[3] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy	SAR245409: Combination Regimen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	37	4
Units: subjects				
Hyperglycemia: All Grades (n=16,3,36,4)	13	3	25	1
Hyperglycemia: Grade 1 (n=16,3,36,4)	11	2	19	1
Hyperglycemia: Grade 2 (n=16,3,36,4)	0	1	6	0
Hyperglycemia: Grade 3 (n=16,3,36,4)	2	0	0	0
Hyperglycemia: Grade 4 (n=16,3,36,4)	0	0	0	0
ASAT Increased: All Grades (n=16,3,36,4)	7	2	20	1
ASAT Increased: Grade 1 (n=16,3,36,4)	6	1	16	1
ASAT Increased: Grade 2 (n=16,3,36,4)	1	1	2	0
ASAT Increased: Grade 3 (n=16,3,36,4)	0	0	2	0
ASAT Increased: Grade 4 (n=16,3,36,4)	0	0	0	0

ALAT Increased: All Grades (n=16,3,36,4)	5	2	12	0
ALAT Increased: Grade 1 (n=16,3,36,4)	4	1	8	0
ALAT Increased: Grade 2 (n=16,3,36,4)	1	1	1	0
ALAT Increased: Grade 3 (n=16,3,36,4)	0	0	3	0
ALAT Increased: Grade 4 (n=16,3,36,4)	0	0	0	0
Blood Bilirubin Increased:All Grades(n=15,3,36,4)	1	0	9	1
Blood Bilirubin Increased:Grade 1(n=15,3,36,4)	0	0	4	1
Blood Bilirubin Increased:Grade 2(n=15,3,36,4)	0	0	3	0
Blood Bilirubin Increased:Grade 3(n=15,3,36,4)	1	0	2	0
Blood Bilirubin Increased:Grade 4(n=15,3,36,4)	0	0	0	0
Hypocalcemia: All Grades (n=16,3,36,4)	6	1	7	0
Hypocalcemia: Grade 1 (n=16,3,36,4)	4	1	5	0
Hypocalcemia: Grade 2 (n=16,3,36,4)	1	0	0	0
Hypocalcemia: Grade 3 (n=16,3,36,4)	1	0	2	0
Hypocalcemia: Grade 4 (n=16,3,36,4)	0	0	0	0
Creatinine increased: All Grades (n=16,3,36,4)	5	1	15	0
Creatinine increased: Grade 1 (n=16,3,36,4)	3	1	8	0
Creatinine increased: Grade 2 (n=16,3,36,4)	1	0	4	0
Creatinine increased: Grade 3 (n=16,3,36,4)	0	0	2	0
Creatinine increased: Grade 4 (n=16,3,36,4)	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from the date of signing the consent up to 30 days after the last dose (maximum of 1959 days) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs and deaths are TEAEs that is AEs and deaths that developed/worsened during the 'on treatment period' (time from the first dose of any study drug up to 30 days after the last dose of any study drug). Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	SAR245408: Monotherapy

Reporting group description:

Subjects received SAR245408 400 mg once daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days).

Reporting group title	SAR245408: Combination Regimen

Reporting group description:

Subjects received SAR245408 400 mg once daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245408 were available (up to 1959 days). Commercially available drugs were used as combination medications with SAR245408 (depending on the parental study, the following drugs were used in combination with SAR245408: paclitaxel and carboplatin, letrozole, trastuzumab, paclitaxel and trastuzumab).

Reporting group title	SAR245409: Monotherapy

Reporting group description:

Subjects received SAR245409 50 mg twice daily or at the established dose as monotherapy in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days).

Reporting group title	SAR245409: Combination Regimen

Reporting group description:

Subjects received SAR245409 50 mg twice daily or at the established dose as combination regimen in the parental study until disease progression, unacceptable toxicity, withdrawal of consent, or until commercial supplies of SAR245409 were available (up to 1917 days). Commercially available drugs were used as combination medications with SAR245409 (depending on the parental study, the following drugs were used in combination with SAR245409: letrozole, temozolomide, rituximab, bendamustine and rituximab).

Serious adverse events	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 17 (52.94%)	1 / 3 (33.33%)	10 / 37 (27.03%)
number of deaths (all causes)	1	0	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Acute Leukaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myeloid Leukaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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			
Haematoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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 disorders and administration site conditions			
Disease Progression			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic Inflammatory Response Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (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
Respiratory Distress			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Angina Unstable			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage Intracranial			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (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
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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 disorders			
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis Acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
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 Acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
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 and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal Colic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Sinusitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter Site Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Discitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
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	2 / 17 (11.76%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal Skin Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (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
Urinary Tract Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
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 Lysis Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SAR245409: Combination Regimen		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Leukaemia			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute Myeloid Leukaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Haematoma				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Disease Progression				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic Inflammatory Response Syndrome				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic Obstructive Pulmonary Disease				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural Effusion				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Distress				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine Aminotransferase Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Troponin Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur Fracture				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
Angina Unstable			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage Intracranial			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal Obstruction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis Acute			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis Acute			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Renal Colic			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Catheter Site Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral Discitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Skin Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour Lysis Syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SAR245408: Monotherapy	SAR245408: Combination Regimen	SAR245409: Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 17 (88.24%)	3 / 3 (100.00%)	34 / 37 (91.89%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Tumour Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Vascular disorders			
Brachiocephalic Vein Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Deep Vein Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Flushing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hot Flush			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	5 / 17 (29.41%)	1 / 3 (33.33%)	8 / 37 (21.62%)
occurrences (all)	5	1	8
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Lymphoedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Systolic Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Catheter Site Discharge			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Chest Pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Chills			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Face Oedema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Facial Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	8 / 17 (47.06%)	1 / 3 (33.33%)	8 / 37 (21.62%)
occurrences (all)	9	1	8
Gait Disturbance			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
General Physical Health Deterioration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Localised Oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Mucosal Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Oedema Peripheral			
subjects affected / exposed	3 / 17 (17.65%)	1 / 3 (33.33%)	4 / 37 (10.81%)
occurrences (all)	3	1	4
Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Performance Status Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Peripheral Swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	4 / 17 (23.53%)	1 / 3 (33.33%)	6 / 37 (16.22%)
occurrences (all)	4	1	6
Suprapubic Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Immune system disorders			
Contrast Media Allergy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Drug Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Prostatic Obstruction			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Testicular Swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Atelectasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 17 (0.00%)	2 / 3 (66.67%)	8 / 37 (21.62%)
occurrences (all)	0	2	8
Dysphonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Dyspnoea			
subjects affected / exposed	3 / 17 (17.65%)	1 / 3 (33.33%)	3 / 37 (8.11%)
occurrences (all)	3	1	3
Dyspnoea Exertional			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Hypoxia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Nasal Congestion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Oropharyngeal Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	3	0	2
Paranasal Sinus Discomfort			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pleural Effusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Pneumonitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Productive Cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	4
Rhinitis Allergic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Rhinorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Tachypnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Tonsillar Inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 17 (23.53%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	4	0	4
Confusional State			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Depression			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	2	0	3
Emotional Distress			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Post-Traumatic Stress Disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Investigations			
Activated Partial Thromboplastin Time Prolonged			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	3	0	0
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 17 (0.00%)	2 / 3 (66.67%)	4 / 37 (10.81%)
occurrences (all)	0	2	5
Amylase Increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	6 / 37 (16.22%)
occurrences (all)	1	0	6
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 17 (0.00%)	2 / 3 (66.67%)	3 / 37 (8.11%)
occurrences (all)	0	2	3
Bilirubin Conjugated Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Blood Bilirubin Increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood Cholesterol Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood Creatinine Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood Phosphorus Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood Urea Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Body Temperature Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Breath Sounds Abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Breath Sounds Absent			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cardiac Murmur			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Chest X-Ray Abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Electrocardiogram Qt Prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2

Heart Rate Irregular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
International Normalised Ratio Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Lipase Increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	8 / 37 (21.62%)
occurrences (all)	2	0	8
Neutrophil Count Decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Nuclear Magnetic Resonance Imaging Brain Abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Platelet Count Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Procalcitonin Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Protein Urine Present			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Prothrombin Time Prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Red Blood Cell Count Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Red Blood Cells Urine			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Urine Analysis Abnormal			

subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Urine Protein/Creatinine Ratio Increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Vitamin B12 Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Vitamin D Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Weight Decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	1	0	4
Weight Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
White Blood Cell Count Decreased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	1 / 37 (2.70%)
occurrences (all)	2	1	1
White Blood Cell Count Increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
White Blood Cells Urine			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
White Blood Cells Urine Positive			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Contusion			

subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	2	0	3
Foreign Body In Eye			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Incision Site Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Ligament Injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Limb Injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Muscle Strain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Rib Fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Skin Abrasion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Spinal Compression Fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Wound Dehiscence			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2

Cardiac Arrest			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cardiomegaly			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Coronary Artery Disease			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Pericardial Effusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Sinus Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Ventricular Extrasystoles			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Ventricular Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Aphasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Ataxia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cognitive Disorder			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 17 (17.65%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	3	0	2
Dizziness Postural			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Dysarthria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	6 / 37 (16.22%)
occurrences (all)	1	0	6
Hypoaesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Lethargy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Memory Impairment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Neuropathy Peripheral			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Partial Seizures			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 17 (0.00%)	2 / 3 (66.67%)	2 / 37 (5.41%)
occurrences (all)	0	2	2
Sciatica			

subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Visual Field Defect			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 17 (17.65%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	4	1	2
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Splenomegaly			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Thrombocytopenia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	3	0	0
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Deafness Unilateral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Ear Discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hyperacusis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hypoacusis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Tinnitus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Eye disorders			
Cataract			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Corneal Scar			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Dry Eye			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Retinal Vein Occlusion			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Visual Impairment			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Vitreous Floaters			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Abdominal Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Abdominal Pain Lower			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Abdominal Tenderness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Abdominal Wall Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Anal Incontinence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Chapped Lips			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	4 / 17 (23.53%)	1 / 3 (33.33%)	7 / 37 (18.92%)
occurrences (all)	4	1	7

Diarrhoea			
subjects affected / exposed	7 / 17 (41.18%)	2 / 3 (66.67%)	14 / 37 (37.84%)
occurrences (all)	8	2	14
Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Faeces Discoloured			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	3 / 17 (17.65%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	4	0	2
Hypoaesthesia Oral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	5 / 17 (29.41%)	2 / 3 (66.67%)	10 / 37 (27.03%)
occurrences (all)	5	2	10
Pancreatic Failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Peptic Ulcer Haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Salivary Gland Enlargement			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Short-Bowel Syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0

Vomiting			
subjects affected / exposed	2 / 17 (11.76%)	2 / 3 (66.67%)	7 / 37 (18.92%)
occurrences (all)	2	2	7
Skin and subcutaneous tissue disorders			
Actinic Keratosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Blister			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Decubitus Ulcer			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Dermatitis Acneiform			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Dry Skin			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Erythema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Ingrowing Nail			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Nail Pigmentation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Night Sweats			

subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	2	0	3
Onychoclasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Pain Of Skin			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Photosensitivity Reaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Precancerous Skin Lesion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 17 (5.88%)	2 / 3 (66.67%)	2 / 37 (5.41%)
occurrences (all)	1	2	2
Pruritus Generalised			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Psoriasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Rash Generalised			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1

Rash Macular			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Rash Maculo-Papular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rash Pruritic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Scab			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Skin Hyperpigmentation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Skin Lesion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Skin Mass			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Swelling Face			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Chronic Kidney Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Dysuria			

subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Glycosuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Haemoglobinuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Hydronephrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Micturition Urgency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Nephrolithiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Nocturia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Oliguria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Proteinuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Renal Failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Urinary Hesitation			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Urinary Incontinence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Urinary Retention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Urinary Tract Pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Urine Flow Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Back Pain			
subjects affected / exposed	4 / 17 (23.53%)	1 / 3 (33.33%)	4 / 37 (10.81%)
occurrences (all)	4	1	4
Bursitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Flank Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Groin Pain			

subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Joint Swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Muscle Spasms			
subjects affected / exposed	3 / 17 (17.65%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	3	0	1
Muscle Twitching			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Muscular Weakness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Musculoskeletal Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Neck Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Osteoporosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pain In Extremity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Pain In Jaw			

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pathological Fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Periarthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Pubic Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Scoliosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Infections and infestations			
Abscess Limb			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	1	0	5
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Chronic Sinusitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Eye Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Fungal Skin Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Gastrointestinal Viral Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Hepatitis C			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Herpes Zoster			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Onychomycosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Oral Candidiasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Postoperative Wound Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Respiratory Tract Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	5 / 37 (13.51%)
occurrences (all)	1	0	5
Skin Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Tooth Abscess			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Tooth Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 17 (17.65%)	0 / 3 (0.00%)	8 / 37 (21.62%)
occurrences (all)	3	0	8
Urinary Tract Infection			
subjects affected / exposed	2 / 17 (11.76%)	1 / 3 (33.33%)	6 / 37 (16.22%)
occurrences (all)	2	1	6
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Decreased Appetite			

subjects affected / exposed	2 / 17 (11.76%)	1 / 3 (33.33%)	5 / 37 (13.51%)
occurrences (all)	2	1	5
Dehydration			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Diabetes Mellitus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Hyperkalaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Hyperlipidaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Hypocalcaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Hypokalaemia			

subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Hypomagnesaemia			
subjects affected / exposed	3 / 17 (17.65%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	3	0	1
Hyponatraemia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	3	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Metabolic Acidosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Vitamin D Deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

Non-serious adverse events	SAR245409: Combination Regimen		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tumour Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Brachiocephalic Vein Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Deep Vein Thrombosis			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hot Flush			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Systolic Hypertension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter Site Discharge			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Face Oedema			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Facial Pain				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Fatigue				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gait Disturbance				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
General Physical Health Deterioration				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Localised Oedema				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Malaise				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Mucosal Inflammation				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Non-Cardiac Chest Pain				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Oedema Peripheral				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pain				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Performance Status Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Peripheral Swelling				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Suprapubic Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Contrast Media Allergy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Drug Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Prostatic Obstruction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Testicular Swelling			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dysphonia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dyspnoea				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dyspnoea Exertional				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypoxia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nasal Congestion				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Oropharyngeal Pain				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Paranasal Sinus Discomfort				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pleural Effusion				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pneumonitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Productive Cough				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rhinitis Allergic				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rhinorrhoea				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tonsillar Inflammation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Confusional State			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Emotional Distress			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Post-Traumatic Stress Disorder			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Investigations			
Activated Partial Thromboplastin Time Prolonged			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Amylase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Bilirubin Conjugated Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Bilirubin Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Cholesterol Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Creatinine Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Phosphorus Decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Blood Urea Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Body Temperature Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Breath Sounds Abnormal				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Breath Sounds Absent				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Cardiac Murmur				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Chest X-Ray Abnormal				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Electrocardiogram Qt Prolonged				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Heart Rate Irregular				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
International Normalised Ratio Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Lipase Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Neutrophil Count Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nuclear Magnetic Resonance Imaging Brain Abnormal				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Platelet Count Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Procalcitonin Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Protein Urine Present				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Prothrombin Time Prolonged				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Red Blood Cell Count Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Red Blood Cells Urine				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urine Analysis Abnormal				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urine Protein/Creatinine Ratio Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Vitamin B12 Increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Vitamin D Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Weight Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			

Weight Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
White Blood Cell Count Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
White Blood Cells Urine			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
White Blood Cells Urine Positive			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Foreign Body In Eye			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Incision Site Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ligament Injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Limb Injury			

subjects affected / exposed occurrences (all) Muscle Strain subjects affected / exposed occurrences (all) Rib Fracture subjects affected / exposed occurrences (all) Skin Abrasion subjects affected / exposed occurrences (all) Spinal Compression Fracture subjects affected / exposed occurrences (all) Wound Dehiscence subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all) Cardiac Arrest subjects affected / exposed occurrences (all) Cardiomegaly subjects affected / exposed occurrences (all) Coronary Artery Disease subjects affected / exposed occurrences (all) Pericardial Effusion subjects affected / exposed occurrences (all) Sinus Bradycardia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		

Tachycardia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Ventricular Extrasystoles				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Ventricular Tachycardia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nervous system disorders				
Amnesia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Aphasia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Ataxia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Cognitive Disorder				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dizziness				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Dizziness Postural				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dysarthria				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypoaesthesia				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Memory Impairment			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neuropathy Peripheral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Partial Seizures			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Seizure			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Visual Field Defect			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Splenomegaly			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Deafness Unilateral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ear Discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperacusis			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoacusis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Corneal Scar			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dry Eye			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Retinal Vein Occlusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Visual Impairment			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vitreous Floaters			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal Pain			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Abdominal Pain Lower				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Abdominal Tenderness				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Abdominal Wall Haematoma				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Anal Incontinence				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Ascites				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Chapped Lips				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Diarrhoea				
subjects affected / exposed	3 / 4 (75.00%)			
occurrences (all)	3			
Dyspepsia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Faeces Discoloured				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Flatulence				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia Oral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pancreatic Failure			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Peptic Ulcer Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Salivary Gland Enlargement			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Short-Bowel Syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Actinic Keratosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Decubitus Ulcer				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dermatitis Acneiform				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dry Skin				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Erythema				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hyperhidrosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Ingrowing Nail				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nail Pigmentation				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Night Sweats				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Onychoclasis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pain Of Skin				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Palmar-Plantar Erythrodysaesthesia Syndrome				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Petechiae				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Photosensitivity Reaction				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Precancerous Skin Lesion				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pruritus Generalised				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Psoriasis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rash				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rash Generalised				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rash Macular				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rash Maculo-Papular				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rash Pruritic				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Scab				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Seborrhoeic Dermatitis				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin Hyperpigmentation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin Lesion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin Mass			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Swelling Face			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Chronic Kidney Disease			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Glycosuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haemoglobinuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hydronephrosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Micturition Urgency				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nephrolithiasis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nocturia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Oliguria				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pollakiuria				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Proteinuria				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Renal Failure				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urinary Hesitation				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urinary Incontinence				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urinary Retention				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urinary Tract Pain				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Urine Flow Decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Back Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Bursitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Flank Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Groin Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Joint Swelling			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscle Spasms			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscle Twitching			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscular Weakness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal Chest Pain			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neck Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain In Extremity			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain In Jaw			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pathological Fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Periarthritis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pubic Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Scoliosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Abscess Limb				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Chronic Sinusitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Eye Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Fungal Skin Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gastrointestinal Viral Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hepatitis C				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Herpes Zoster				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			

Influenza				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Lower Respiratory Tract Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Onychomycosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Oral Candidiasis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Postoperative Wound Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Respiratory Tract Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Sepsis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Skin Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			

Tooth Abscess			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tooth Infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Urinary Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Decreased Appetite			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Diabetes Mellitus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hyperglycaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hyperkalaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hyperlipidaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hyperphosphataemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypoalbuminaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypocalcaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypokalaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypomagnesaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hyponatraemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hypophosphataemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Metabolic Acidosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Vitamin D Deficiency				

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2012	Following amendments were made: - To update name and addresses of Clinical Study Director, Clinical Trial Operation Manager, and Emergency contact information on cover page. -To add SAR245408 tablet formulation with polymorph E in sections Clinical Trial Summary: study design, study treatment(s): formulation, dose regimen, pharmaceutical form, dose preparation and administration, extent of study treatment exposure. -To clarify entery into the treatment extension study time point in sections Graphical study design, study flowchart for SAR245408 or SAR245409 treatment, description of the protocol, Duration of study participation for each subject, visit schedule. -To change inclusion and exclusion criteria to have them aligned with treatment continuation criteria of parental protocols. - To correct pharmaceutical form of polymorph tablet A, the tablet is not film coated. - To clarify fasting requirements for subjects taking SAR245408 tablet polymorph E. - To update of the AEs reporting instruction, clarification of language for general guidelines for reporting AEs. - Minor editorial updates in Pretreatment period.
16 June 2014	To update information regarding changes in the available formulation and dosage strengths of the investigational medicinal products. - To change recommendations for transition of ongoing subjects from SAR245408 (form A) hard capsules or (form A) tablets to (form E) film-coated tablets. - To recommend management of ongoing subjects once the supply of SAR245409A 10 mg (lowest available strength) hard capsules was depleted. Ongoing subjects whose dose had included the 10 mg capsule strength was offered continuation of treatment at a comparable dose level with a revised schedule in consultation with the sponsor. This change only affected subjects needing a further dose reduction below 30 mg. For example, subjects unable to tolerate 30 mg capsules twice a day (BID) may be permitted to take 30 mg capsules once daily (QD). Treatment was discontinued for subjects who could not tolerate 30 mg capsules QD. - To clarify that reporting of skin toxicities as adverse event with special interest (AESI) was required only if the event is >= grade 2. - To indicate that additional reasons the sponsor may terminate the study include drug supply or manufacturing issues and the sponsor’s decision to discontinue the development of the IMP. - To revise the schedule of procedures to require 12-lead ECG every 12 weeks and as clinically indicated during the Extension Period, rather than every 4-6 weeks. This examination frequency was considered clinically appropriate based on the lack of evidence of cardiac toxicity in clinical studies of SAR245408 and SAR245409. - To update sponsor personnel contact information. - Administrative corrections/revisions throughout the document were made for clarity and/or internal consistency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported