



## 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
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##### 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:

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**Results analysis stage**

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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:

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**General information about the trial**

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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:

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**Population of trial subjects**

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**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:

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**Subjects enrolled per age group**

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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  $\geq$ 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
<b>Arm title</b>	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.

<b>Arm title</b>	SAR245408: Combination Regimen
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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.

<b>Arm title</b>	SAR245409: Monotherapy
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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.

<b>Arm title</b>	SAR245409: Combination Regimen
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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
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
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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
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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
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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
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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 standard deviation	61.6 ± 13.1	53.7 ± 2.1	62.4 ± 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

<b>Reporting group values</b>	SAR245409: Combination Regimen	Total	
Number of subjects	4	61	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	50.0 ± 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) <sup>[1]</sup>
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.

<b>End point values</b>	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 <sup>[2]</sup>
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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
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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.

<b>End point values</b>	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 <sup>[3]</sup>
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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
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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

Reporting group title	SAR245408: Monotherapy
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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
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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
<b>Dyspnoea</b>			
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
<b>Pleural Effusion</b>			
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
<b>Respiratory Distress</b>			
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
<b>Investigations</b>			
<b>Alanine Aminotransferase Increased</b>			
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
<b>Lipase Increased</b>			
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
<b>Troponin Increased</b>			
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
<b>Injury, poisoning and procedural complications</b>			
<b>Femur Fracture</b>			
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
<b>Gastrointestinal disorders</b>			
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
<b>Hepatobiliary disorders</b>			
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
<b>Renal and urinary disorders</b>			
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
<b>Staphylococcal Skin Infection</b>			
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
<b>Urinary Tract Infection</b>			
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
<b>Wound Infection</b>			
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
<b>Metabolism and nutrition disorders</b>			
<b>Hypercalcaemia</b>			
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
<b>Tumour Lysis Syndrome</b>			
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

<b>Serious adverse events</b>	SAR245409: Combination Regimen		
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
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		
<b>Dyspnoea</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Pleural Effusion</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory Distress</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Investigations</b>			
<b>Alanine Aminotransferase Increased</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Lipase Increased</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Troponin Increased</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Injury, poisoning and procedural complications</b>			
<b>Femur Fracture</b>			
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		
<b>Gastrointestinal disorders</b>			
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		
<b>Hepatobiliary disorders</b>			
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		
<b>Renal and urinary disorders</b>			
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		
<b>Staphylococcal Skin Infection</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Urinary Tract Infection</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Wound Infection</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Metabolism and nutrition disorders</b>			
<b>Hypercalcaemia</b>			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Tumour Lysis Syndrome</b>			
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 %

<b>Non-serious adverse events</b>	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 occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	3 / 37 (8.11%) 3
Oedema Peripheral subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	1 / 3 (33.33%) 1	4 / 37 (10.81%) 4
Pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Performance Status Decreased subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Peripheral Swelling subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Pyrexia subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 4	1 / 3 (33.33%) 1	6 / 37 (16.22%) 6
Suprapubic Pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Immune system disorders Contrast Media Allergy subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Drug Hypersensitivity subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Hypersensitivity subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Reproductive system and breast disorders Benign Prostatic Hyperplasia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 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
<b>Pleural Effusion</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
<b>Pneumonitis</b>			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
<b>Productive Cough</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	4
<b>Rhinitis Allergic</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
<b>Rhinorrhoea</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
<b>Sleep Apnoea Syndrome</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Tachypnoea</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Tonsillar Inflammation</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Wheezing</b>			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
<b>Psychiatric disorders</b>			
<b>Anxiety</b>			
subjects affected / exposed	4 / 17 (23.53%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	4	0	4
<b>Confusional State</b>			
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 occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 3 (0.00%) 0	3 / 37 (8.11%) 3
Foreign Body In Eye subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Incision Site Pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Ligament Injury subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Limb Injury subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Muscle Strain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	2 / 37 (5.41%) 2
Rib Fracture subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Skin Abrasion subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Spinal Compression Fracture subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 3 (33.33%) 1	0 / 37 (0.00%) 0
Wound Dehiscence subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 3 (33.33%) 1	0 / 37 (0.00%) 0
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	2 / 37 (5.41%) 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 occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Seizure subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Syncope subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Visual Field Defect subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
<b>Blood and lymphatic system disorders</b>			
Anaemia subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 4	1 / 3 (33.33%) 1	2 / 37 (5.41%) 2
Iron Deficiency Anaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Leukocytosis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Leukopenia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Lymphopenia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Neutropenia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	2 / 37 (5.41%) 2
Splenomegaly subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1

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

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Visual Impairment subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Vitreous Floaters subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
<b>Gastrointestinal disorders</b>			
Abdominal Distension subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	2 / 37 (5.41%) 2
Abdominal Pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	3 / 37 (8.11%) 3
Abdominal Pain Lower subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Abdominal Tenderness subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Abdominal Wall Haematoma subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Anal Incontinence subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Ascites subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Chapped Lips subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 4	1 / 3 (33.33%) 1	7 / 37 (18.92%) 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
Gastroesophageal 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
<b>Skin and subcutaneous tissue disorders</b>			
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
<b>Onychoclasia</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Pain Of Skin</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Palmar-Plantar Erythrodysesthesia Syndrome</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Petechiae</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Photosensitivity Reaction</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Precancerous Skin Lesion</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Pruritus</b>			
subjects affected / exposed	1 / 17 (5.88%)	2 / 3 (66.67%)	2 / 37 (5.41%)
occurrences (all)	1	2	2
<b>Pruritus Generalised</b>			
subjects affected / exposed	1 / 17 (5.88%)	1 / 3 (33.33%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
<b>Psoriasis</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Rash</b>			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
<b>Rash Generalised</b>			
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
<b>Glycosuria</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Haematuria</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
<b>Haemoglobinuria</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Hydronephrosis</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
<b>Micturition Urgency</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
<b>Nephrolithiasis</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
<b>Nocturia</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Oliguria</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Pollakiuria</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
<b>Proteinuria</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
<b>Renal Failure</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Urinary Hesitation</b>			

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

subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Pathological Fracture</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Periarthritis</b>			
subjects affected / exposed	0 / 17 (0.00%)	1 / 3 (33.33%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
<b>Pubic Pain</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Scoliosis</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
<b>Infections and infestations</b>			
<b>Abscess Limb</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Bronchitis</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	4 / 37 (10.81%)
occurrences (all)	1	0	5
<b>Cellulitis</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Chronic Sinusitis</b>			
subjects affected / exposed	2 / 17 (11.76%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
<b>Conjunctivitis</b>			
subjects affected / exposed	1 / 17 (5.88%)	0 / 3 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
<b>Eye Infection</b>			
subjects affected / exposed	0 / 17 (0.00%)	0 / 3 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
<b>Fungal Skin Infection</b>			
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 occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Sepsis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Sinusitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	5 / 37 (13.51%) 5
Skin Infection subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	2 / 37 (5.41%) 2
Tooth Abscess subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Tooth Infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	0 / 3 (0.00%) 0	8 / 37 (21.62%) 8
Urinary Tract Infection subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	1 / 3 (33.33%) 1	6 / 37 (16.22%) 6
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 3 (0.00%) 0	0 / 37 (0.00%) 0
Metabolism and nutrition disorders			
Acidosis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 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 occurrences (all)	1 / 17 (5.88%) 1	1 / 3 (33.33%) 1	2 / 37 (5.41%) 2
Hypomagnesaemia subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Hyponatraemia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 3	0 / 3 (0.00%) 0	2 / 37 (5.41%) 2
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	2 / 37 (5.41%) 2
Metabolic Acidosis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1
Vitamin D Deficiency subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 3 (0.00%) 0	1 / 37 (2.70%) 1

<b>Non-serious adverse events</b>	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 occurrences (all)	0 / 4 (0.00%) 0		
Squamous Cell Carcinoma Of Skin subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Tumour Pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vascular disorders Brachiocephalic Vein Thrombosis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Deep Vein Thrombosis			

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

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

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

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

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

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Muscle Strain</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Rib Fracture</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Skin Abrasion</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Spinal Compression Fracture</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Wound Dehiscence</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Cardiac disorders</b>			
<b>Bradycardia</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Cardiac Arrest</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Cardiomegaly</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Coronary Artery Disease</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Pericardial Effusion</b> subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
<b>Sinus Bradycardia</b> subjects affected / exposed occurrences (all)	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 occurrences (all)	0 / 4 (0.00%) 0		
Hypoacusis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Tinnitus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vertigo subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Corneal Scar subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Dry Eye subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Retinal Vein Occlusion subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Visual Impairment subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vitreous Floaters subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Gastrointestinal disorders Abdominal Distension subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Abdominal Pain			

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

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

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

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin Hyperpigmentation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin Lesion subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin Mass subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Swelling Face subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Renal and urinary disorders			
Chronic Kidney Disease subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Dysuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Glycosuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Haematuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Haemoglobinuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 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 occurrences (all)	0 / 4 (0.00%) 0		
Musculoskeletal Pain			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Myalgia			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Neck Pain			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Osteoarthritis			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Osteoporosis			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pain In Extremity			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pain In Jaw			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pathological Fracture			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Periarthritis			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pubic Pain			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Scoliosis			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 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		

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

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

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

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2012	<p>Following amendments were made: - To update name and addresses of Clinical Study Director, Clinical Trial Operation Manager, and Emergency contact information on cover page.</p> <ul style="list-style-type: none"><li>-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.</li><li>-To clarify entry 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.</li><li>-To change inclusion and exclusion criteria to have them aligned with treatment continuation criteria of parental protocols.</li><li>- To correct pharmaceutical form of polymorph tablet A, the tablet is not film coated.</li><li>- To clarify fasting requirements for subjects taking SAR245408 tablet polymorph E.</li><li>- To update of the AEs reporting instruction, clarification of language for general guidelines for reporting AEs.</li><li>- Minor editorial updates in Pretreatment period.</li></ul>
16 June 2014	<p>To update information regarding changes in the available formulation and dosage strengths of the investigational medicinal products.</p> <ul style="list-style-type: none"><li>- To change recommendations for transition of ongoing subjects from SAR245408 (form A) hard capsules or (form A) tablets to (form E) film-coated tablets.</li><li>- 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.</li><li>- To clarify that reporting of skin toxicities as adverse event with special interest (AESI) was required only if the event is <math>\geq</math> grade 2.</li><li>- 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.</li><li>- 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.</li><li>- To update sponsor personnel contact information.</li><li>- Administrative corrections/revisions throughout the document were made for clarity and/or internal consistency.</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported