



Clinical trial results:

Phase III trial comparing conventional adjuvant temozolomide with dose-intensive temozolomide in patients with newly diagnosed glioblastoma

Summary

EudraCT number	2005-005177-29
Trial protocol	DE BE GB FR LV NL SI
Global end of trial date	01 December 2016

Results information

Result version number	v1 (current)
This version publication date	29 August 2021
First version publication date	29 August 2021

Trial information

Trial identification

Sponsor protocol code	EORTC 26052-22053
-----------------------	-------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00304031
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	RTOG Foundation
Sponsor organisation address	50 South 16th Street, Suite 2800, Philadelphia, United States, 19102
Public contact	RTOG Foundation, RTOG Foundation, info@rtog.org
Scientific contact	RTOG Foundation, RTOG Foundation, 2155743173 2155743173, info@rtog.org

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 February 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2011
Global end of trial reached?	Yes
Global end of trial date	01 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if dose-intensifying (increase the 'dose-density') the adjuvant temozolomide component of the chemoradiation treatment enhances treatment efficacy as measured by overall survival

Protection of trial subjects:

RTOG DMC reviewed the accrual to the study and the rate of adverse events on the study at least twice a year until the initial results of the study have been presented to the scientific community. The efficacy results of this study were reviewed by the RTOG DMC four times

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 26
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	United States: 935
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	United Kingdom: 77
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Latvia: 29
Worldwide total number of subjects	1125
EEA total number of subjects	80

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	375
From 65 to 84 years	375
85 years and over	375

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Registered participants had to have MGMT (O-6-methylguanine-DNA methyltransferase) status determination in order for them to continue on the study. Of 1173 participants initially registered, 1125 participants met these requirements and started protocol treatment. 833 patients were randomized.

Pre-assignment period milestones

Number of subjects started	1125
Number of subjects completed	833

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Disease progression: 48
Reason: Number of subjects	Ineligible due to insufficient tissue: 144
Reason: Number of subjects	Consent withdrawn by subject: 19
Reason: Number of subjects	Death: 18
Reason: Number of subjects	Physician decision: 15
Reason: Number of subjects	Adverse event, non-fatal: 10
Reason: Number of subjects	Other complicating disease: 1
Reason: Number of subjects	Other, not otherwise specified: 37

Period 1

Period 1 title	Randomization (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Conventional Adjuvant TMZ

Arm description:

Concurrent radiation therapy with concurrent temozolomide (75 mg/m²) up to 49 doses. Starting four weeks after completion of RT, 100mg/m² adjuvant temozolomide days 1 to 5 of 28 day cycle.

Arm type	Active comparator
----------	-------------------

Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder in single-dose container
Routes of administration	Oral use

Dosage and administration details:

(75 mg/m²) up to 49 doses. Starting four weeks after completion of RT, 100mg/m² adjuvant temozolomide days 1 to 5 of 28 day cycle.

Arm title	Dose-dense Adjuvant TMZ
------------------	-------------------------

Arm description:

Concurrent radiation therapy (RT) with concurrent temozolomide (75 mg/m²) up to 49 doses. Starting four weeks after completion of RT, 75mg/m² adjuvant temozolomide days 1-21 of 28 day cycle.

Arm type	Experimental
Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder in single-dose container
Routes of administration	Oral use

Dosage and administration details:

(75 mg/m²) up to 49 doses. Starting four weeks after completion of RT, 75mg/m² adjuvant temozolomide days 1-21 of 28 day cycle.

Number of subjects in period 1 ^[1]	Conventional Adjuvant TMZ	Dose-dense Adjuvant TMZ
Started	411	422
Completed	411	420
Not completed	0	2
No follow-up collected	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1173 patient were first registered, 1125 could start RT and concomitant TMZ. Adjuvant TMZ could start for 833 patients which were randomized between the two treatment arms. The dropout

reasons are explained in the pre-assignment section.

Baseline characteristics

Reporting groups

Reporting group title	Conventional Adjuvant TMZ
Reporting group description:	
Concurrent radiation therapy with concurrent temozolomide (75 mg/m2) up to 49 doses. Starting four weeks after completion of RT, 100mg/m2 adjuvant temozolomide days 1 to 5 of 28 day cycle.	
Reporting group title	Dose-dense Adjuvant TMZ
Reporting group description:	
Concurrent radiation therapy (RT) with concurrent temozolomide (75 mg/m2) up to 49 doses. Starting four weeks after completion of RT, 75mg/m2 adjuvant temozolomide days 1-21 of 28 day cycle.	

Reporting group values	Conventional Adjuvant TMZ	Dose-dense Adjuvant TMZ	Total
Number of subjects	411	422	833
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	307	326	633
From 65-84 years	104	96	200
85 years and over	0	0	0
Age continuous Units: years			
median	57	58	
full range (min-max)	22 to 84	21 to 84	-
Gender categorical Units: Subjects			
Female	172	185	357
Male	239	237	476

End points

End points reporting groups

Reporting group title	Conventional Adjuvant TMZ
Reporting group description: Concurrent radiation therapy with concurrent temozolomide (75 mg/m ²) up to 49 doses. Starting four weeks after completion of RT, 100mg/m ² adjuvant temozolomide days 1 to 5 of 28 day cycle.	
Reporting group title	Dose-dense Adjuvant TMZ
Reporting group description: Concurrent radiation therapy (RT) with concurrent temozolomide (75 mg/m ²) up to 49 doses. Starting four weeks after completion of RT, 75mg/m ² adjuvant temozolomide days 1-21 of 28 day cycle.	

Primary: Overall Survival

End point title	Overall Survival
End point description:	
End point type	Primary
End point timeframe: After treatment, survival information is collected at the conclusion of protocol therapy; then q 3 months x 1 year; then every 4 months x 1 year; then q 6 months. Also at progression/relapse and at death.	

End point values	Conventional Adjuvant TMZ	Dose-dense Adjuvant TMZ		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	420 ^[1]		
Units: month				
median (confidence interval 95%)	16.6 (14.9 to 18.0)	14.9 (13.7 to 16.5)		

Notes:

[1] - For 2 patients no follow-up collected

Statistical analyses

Statistical analysis title	Overall Survival Analysis
Statistical analysis description: This study was looking for a 20% reduction in hazard rate: null hypothesis (conventional arm): Median survival time (MST) = 14.0 mo.; alternative hypothesis (dose-dense arm): MST= 17.5 mo. A onesided log-rank test at a significance level of 0.025 would have 80% power to detect this difference with a sample size of 750 patients (647 deaths were required for the final analysis).	
Comparison groups	Dose-dense Adjuvant TMZ v Conventional Adjuvant TMZ
Number of subjects included in analysis	831
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.2

Secondary: Progression-free Survival

End point title	Progression-free Survival
End point description:	
End point type	Secondary
End point timeframe: MRI was obtained prior to surgery, post-surgery, prior to initiation of the concurrent radiation and temozolomide therapy, then within 72 hours prior to initiating adjuvant chemotherapy, then every 3 cycles, and at the time of neurologic deterioration.	

End point values	Conventional Adjuvant TMZ	Dose-dense Adjuvant TMZ		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	420		
Units: Months				
median (confidence interval 95%)	5.5 (4.7 to 6.1)	6.7 (6.2 to 7.7)		

Statistical analyses

Statistical analysis title	PFS analysis
Comparison groups	Conventional Adjuvant TMZ v Dose-dense Adjuvant TMZ

Number of subjects included in analysis	831
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected on a CRF to be submitted at pre-specified timepoint : (+give the different timepoint)

Adverse event reporting additional description:

CRF for AEs contains pre-specified items + additional boxes for all "other" AEs. (xx% AEs are reported as "other" and are not reported as not available from the list of SOC).

AEs are evaluated using CTC grading, SAEs using MedDra. Non-SAEs has not been collected specifically, all AEs will be reported in non-SAE section.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	CTCAE
Dictionary version	3

Reporting groups

Reporting group title	Conventional Adjuvant TMZ
-----------------------	---------------------------

Reporting group description:

Conventional Adjuvant TMZ

Reporting group title	Dose-dense Adjuvant TMZ
-----------------------	-------------------------

Reporting group description:

Dose-dense Adjuvant TMZ

Serious adverse events	Conventional Adjuvant TMZ	Dose-dense Adjuvant TMZ	
Total subjects affected by serious adverse events			
subjects affected / exposed	126 / 411 (30.66%)	139 / 422 (32.94%)	
number of deaths (all causes)	320	332	
number of deaths resulting from adverse events	6	9	
Vascular disorders			
HEMATOMA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOSIS			
alternative dictionary used: CTCAE			

3			
subjects affected / exposed	15 / 411 (3.65%)	19 / 422 (4.50%)	
occurrences causally related to treatment / all	3 / 16	6 / 22	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
DEATH NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
DISEASE PROGRESSION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 2	
EDEMA: HEAD AND NECK:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EDEMA: LIMB:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	9 / 411 (2.19%)	10 / 422 (2.37%)	
occurrences causally related to treatment / all	13 / 13	9 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
GAIT ABNORMAL NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA-LIKE ILLNESS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	7 / 422 (1.66%)	
occurrences causally related to treatment / all	4 / 5	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
RIGORS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
CYTOKINE RELEASE SYNDROME			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERSENSITIVITY NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ASPIRATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
COUGH			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	7 / 422 (1.66%)	
occurrences causally related to treatment / all	5 / 6	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	6 / 422 (1.42%)	
occurrences causally related to treatment / all	0 / 1	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASAL CAVITY/PARANASAL SINUS REACTIONS:			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 411 (0.97%)	6 / 422 (1.42%)	
occurrences causally related to treatment / all	1 / 4	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY/UPPER RESPIRATORY - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT HEMORRHAGE NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
AGITATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONFUSIONAL STATE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	12 / 411 (2.92%)	8 / 422 (1.90%)	
occurrences causally related to treatment / all	4 / 14	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSION			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	2 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
INSOMNIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERSONALITY CHANGE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSYCHOSIS AGGRAVATED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPARTATE AMINOTRANSFERASE INCREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	3 / 411 (0.73%)	3 / 422 (0.71%)		
occurrences causally related to treatment / all	2 / 3	1 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
BLOOD AMYLASE INCREASED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	1 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
BLOOD BILIRUBIN INCREASED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)		
occurrences causally related to treatment / all	3 / 3	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
BLOOD CREATININE INCREASED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
CD4 LYMPHOCYTES DECREASED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	0 / 411 (0.00%)	6 / 422 (1.42%)		
occurrences causally related to treatment / all	0 / 0	13 / 13		
deaths causally related to treatment / all	0 / 0	0 / 0		
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION				
alternative dictionary used: CTCAE 3				

subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	15 / 411 (3.65%)	14 / 422 (3.32%)	
occurrences causally related to treatment / all	17 / 18	13 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIPASE INCREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHOPENIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	23 / 422 (5.45%)	
occurrences causally related to treatment / all	8 / 8	34 / 35	
deaths causally related to treatment / all	0 / 0	0 / 0	
METABOLIC/LABORATORY - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPHIL COUNT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	15 / 411 (3.65%)	11 / 422 (2.61%)	
occurrences causally related to treatment / all	15 / 16	10 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLATELET COUNT DECREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	20 / 411 (4.87%)	16 / 422 (3.79%)	
occurrences causally related to treatment / all	23 / 24	16 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	

TROPONIN I INCREASED alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
WEIGHT DECREASED alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications FRACTURE NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR ACCESS NOS COMPLICATION alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders ATRIAL FIBRILLATION alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL TACHYCARDIA alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS BRADYCARDIA			

alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS TACHYCARDIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR EXTRASYSTOLES			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ATAXIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL ISCHAEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	4 / 422 (0.95%)	
occurrences causally related to treatment / all	1 / 4	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBROSPINAL FLUID LEAK			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CNS NECROSIS/CYSTIC PROGRESSION:			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COGNITIVE DISORDER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	4 / 422 (0.95%)	
occurrences causally related to treatment / all	1 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
CONVULSIONS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	20 / 411 (4.87%)	24 / 422 (5.69%)	
occurrences causally related to treatment / all	5 / 22	10 / 29	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSED LEVEL OF CONSCIOUSNESS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	1 / 5	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSGEUSIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALOPATHY			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
EXTRAPYRAMIDAL DISORDER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	7 / 422 (1.66%)	
occurrences causally related to treatment / all	3 / 6	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYDROCEPHALUS ACQUIRED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERREFLEXIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MEMORY IMPAIRMENT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	2 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENTAL STATUS CHANGES			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): FACIAL			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEURALGIA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROLOGY - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	4 / 422 (0.95%)	
occurrences causally related to treatment / all	0 / 2	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROPATHY: CRANIAL: CN VIII HEARING AND BALANCE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL MOTOR NEUROPATHY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	7 / 411 (1.70%)	7 / 422 (1.66%)	
occurrences causally related to treatment / all	1 / 8	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL SENSORY NEUROPATHY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPEECH DISORDER			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE VASOVAGAL			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TREMOR			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
BLOOD/BONE MARROW - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE MARROW DEPRESSION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
HAEMOLYSIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMOGLOBIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	5 / 422 (1.18%)	
occurrences causally related to treatment / all	5 / 5	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOTIC MICROANGIOPATHY NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Eye disorders			
DIPLOPIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EXTRAOCULAR MUSCLE DISORDER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OCULAR/VISUAL - OTHER:			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RETINAL DETACHMENT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VISION BLURRED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLONIC PERFORATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	2 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPHAGIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 411 (0.97%)	10 / 422 (2.37%)	
occurrences causally related to treatment / all	4 / 4	8 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

RECTAL HEMORRHAGE alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	8 / 422 (1.90%)	
occurrences causally related to treatment / all	2 / 3	6 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders CHOLECYSTITIS NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC FAILURE alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders ACNE NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DERMATITIS EXFOLIATIVE NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN OF SKIN alternative dictionary used: CTCAE 3			

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PETECHIAE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
CYSTITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY INCONTINENCE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
CUSHINGOID			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	0 / 5	0 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUSCLE WEAKNESS NOS				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	2 / 411 (0.49%)	9 / 422 (2.13%)		
occurrences causally related to treatment / all	2 / 3	5 / 9		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): EXTREMITY-LOWER				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	1 / 2	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): EXTREMITY-UPPER				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): LEFT-SIDED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): RIGHT-SIDED				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)		
occurrences causally related to treatment / all	0 / 1	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
PAIN IN EXTREMITY				

alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	1 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABDOMINAL INFECTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE INFECTION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EYE INFECTION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 411 (0.97%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	5 / 6	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): BILIARY TREE			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): BLADDER (URINARY)				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): KIDNEY				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): LUNG (PNEUMONIA)				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	2 / 411 (0.49%)	4 / 422 (0.95%)		
occurrences causally related to treatment / all	1 / 2	4 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): RECTUM				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: NERVE-PERIPHERAL				
alternative dictionary used: CTCAE 3				
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: WOUND			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION WITH UNKNOWN ANC: LUNG (PNEUMONIA)			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION WITH UNKNOWN ANC: SKIN (CELLULITIS)			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTIOUS MENINGITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
OPPORTUNISITIC INFECTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	5 / 422 (1.18%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	2 / 2	
PNEUMONIA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	3 / 422 (0.71%)	
occurrences causally related to treatment / all	1 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS NOS			

alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN INFECTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	2 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND INFECTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
ACIDOSIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALKALOSIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANOREXIA			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	5 / 422 (1.18%)	
occurrences causally related to treatment / all	2 / 3	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	7 / 422 (1.66%)	
occurrences causally related to treatment / all	1 / 2	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	2 / 422 (0.47%)	
occurrences causally related to treatment / all	1 / 7	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOALBUMINEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	4 / 422 (0.95%)	
occurrences causally related to treatment / all	0 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOGLYCEMIA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	6 / 422 (1.42%)	
occurrences causally related to treatment / all	1 / 3	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOMAGNESEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

HYPONATREMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	1 / 422 (0.24%)	
occurrences causally related to treatment / all	1 / 8	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Conventional Adjuvant TMZ	Dose-dense Adjuvant TMZ	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	383 / 411 (93.19%)	397 / 422 (94.08%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps) SECONDARY MALIGNANCY - POSSIBLY RELATED TO CANCER TREATMENT alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
Vascular disorders FLUSHING alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	2 / 422 (0.47%)	
occurrences (all)	5	2	
HEMATOMA alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	5 / 422 (1.18%)	
occurrences (all)	1	5	
HEMORRHAGE/BLEEDING - OTHER: alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	4 / 422 (0.95%)	
occurrences (all)	3	5	
HOT FLUSHES NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	5 / 422 (1.18%)	
occurrences (all)	8	7	
HYPERTENSION NOS			

alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	7 / 422 (1.66%)	
occurrences (all)	10	15	
HYPOTENSION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	7 / 411 (1.70%)	17 / 422 (4.03%)	
occurrences (all)	7	26	
LYMPHOEDEMA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
PHLEBITIS SUPERFICIAL			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	2 / 422 (0.47%)	
occurrences (all)	2	2	
THROMBOSIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	28 / 411 (6.81%)	33 / 422 (7.82%)	
occurrences (all)	42	40	
VASCULAR - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
CHEST PAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	7 / 411 (1.70%)	10 / 422 (2.37%)	
occurrences (all)	7	10	
CONSTITUTIONAL SYMPTOMS - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	9 / 422 (2.13%)	
occurrences (all)	7	28	
DEATH NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
DISEASE PROGRESSION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)
occurrences (all)	4	3
EDEMA: HEAD AND NECK:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	14 / 411 (3.41%)	26 / 422 (6.16%)
occurrences (all)	24	49
EDEMA: LIMB:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	48 / 411 (11.68%)	53 / 422 (12.56%)
occurrences (all)	91	107
EDEMA: TRUNK/GENITAL:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	2
EDEMA: VISCERA:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
FACIAL PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	2 / 422 (0.47%)
occurrences (all)	6	2
FATIGUE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	291 / 411 (70.80%)	318 / 422 (75.36%)
occurrences (all)	1108	1347
GAIT ABNORMAL NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	15 / 411 (3.65%)	13 / 422 (3.08%)
occurrences (all)	46	28

INFLUENZA-LIKE ILLNESS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	8 / 422 (1.90%)	
occurrences (all)	3	9	
INJECTION SITE REACTION NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
IRRITABILITY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)	
occurrences (all)	2	0	
PAIN - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	27 / 411 (6.57%)	23 / 422 (5.45%)	
occurrences (all)	50	46	
PAIN NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	10 / 411 (2.43%)	8 / 422 (1.90%)	
occurrences (all)	15	9	
PYREXIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	28 / 411 (6.81%)	31 / 422 (7.35%)	
occurrences (all)	34	43	
RIGORS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	13 / 411 (3.16%)	14 / 422 (3.32%)	
occurrences (all)	19	17	
SUDDEN DEATH			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences (all)	0	2	
Immune system disorders			

ALLERGY/IMMUNOLOGY - OTHER: alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	3 / 411 (0.73%) 3	3 / 422 (0.71%) 4	
CYTOKINE RELEASE SYNDROME alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 1	0 / 422 (0.00%) 0	
HYPERSENSITIVITY NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	10 / 411 (2.43%) 13	11 / 422 (2.61%) 14	
Reproductive system and breast disorders BREAST FUNCTION/LACTATION: alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	0 / 411 (0.00%) 0	1 / 422 (0.24%) 1	
ERECTILE DYSFUNCTION NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	3 / 411 (0.73%) 8	2 / 422 (0.47%) 6	
GYNAECOMASTIA alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	0 / 411 (0.00%) 0	1 / 422 (0.24%) 1	
MENSTRUATION IRREGULAR alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	0 / 411 (0.00%) 0	1 / 422 (0.24%) 1	
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): PELVIC alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 1	0 / 422 (0.00%) 0	
SEXUAL/REPRODUCTIVE FUNCTION -			

OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences (all)	1	2	
TESTICULAR PAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
VAGINAL DISCHARGE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences (all)	1	2	
VAGINAL HEMORRHAGE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
ASPIRATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)	
occurrences (all)	3	1	
ATELECTASIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
BRONCHOSPASM			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	5 / 422 (1.18%)	
occurrences (all)	0	7	
COUGH			

alternative dictionary used: CTCAE 3		
subjects affected / exposed	49 / 411 (11.92%)	54 / 422 (12.80%)
occurrences (all)	87	92
DYSпноEA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	38 / 411 (9.25%)	41 / 422 (9.72%)
occurrences (all)	76	83
EPISTAXIS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	8 / 411 (1.95%)	4 / 422 (0.95%)
occurrences (all)	8	8
HICCUPS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	0 / 422 (0.00%)
occurrences (all)	5	0
HYPOXIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	10 / 422 (2.37%)
occurrences (all)	2	15
LARYNGEAL DISCOMFORT		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	3 / 422 (0.71%)
occurrences (all)	0	3
LARYNGITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	7 / 422 (1.66%)
occurrences (all)	3	11
MUCOSITIS/STOMATITIS (CLINICAL EXAM): PHARYNX		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
MUCOSITIS/STOMATITIS (FUNCTIONAL/SYMPTOMATIC): PHARYNX		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
NASAL CAVITY/PARANASAL SINUS REACTIONS:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	7 / 422 (1.66%)
occurrences (all)	1	11
OBSTRUCTION/STENOSIS OF AIRWAY: PHARYNX		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	4
PHARYNGOLARYNGEAL PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	8 / 411 (1.95%)	10 / 422 (2.37%)
occurrences (all)	14	17
PLEURAL EFFUSION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	2	0
PLEURITIC PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
PNEUMONITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	9 / 411 (2.19%)	11 / 422 (2.61%)
occurrences (all)	9	13
PROLONGED CHEST TUBE DRAINAGE OR AIR LEAK AFTER PULMONARY RESECTION:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
PULMONARY/UPPER RESPIRATORY - OTHER:		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	9 / 411 (2.19%)	17 / 422 (4.03%)	
occurrences (all)	10	23	
RESPIRATORY TRACT HEMORRHAGE NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
RHINITIS ALLERGIC NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 411 (0.97%)	13 / 422 (3.08%)	
occurrences (all)	8	28	
Psychiatric disorders			
AGITATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	26 / 411 (6.33%)	14 / 422 (3.32%)	
occurrences (all)	44	19	
ANXIETY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	48 / 411 (11.68%)	41 / 422 (9.72%)	
occurrences (all)	96	100	
CONFUSIONAL STATE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	63 / 411 (15.33%)	61 / 422 (14.45%)	
occurrences (all)	102	97	
DEPRESSION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	54 / 411 (13.14%)	61 / 422 (14.45%)	
occurrences (all)	112	138	
EUPHORIC MOOD			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
INSOMNIA			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	84 / 411 (20.44%)	75 / 422 (17.77%)	
occurrences (all)	163	148	
LIBIDO DECREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	3 / 422 (0.71%)	
occurrences (all)	4	6	
PERSONALITY CHANGE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	18 / 411 (4.38%)	13 / 422 (3.08%)	
occurrences (all)	26	16	
PSYCHOSIS AGGRAVATED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	7 / 422 (1.66%)	
occurrences (all)	8	7	
Investigations			
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	6 / 422 (1.42%)	
occurrences (all)	2	14	
ALANINE AMINOTRANSFERASE INCREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	102 / 411 (24.82%)	111 / 422 (26.30%)	
occurrences (all)	235	250	
ASPARTATE AMINOTRANSFERASE INCREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	65 / 411 (15.82%)	71 / 422 (16.82%)	
occurrences (all)	114	124	
BLOOD ALKALINE PHOSPHATASE INCREASED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	46 / 411 (11.19%)	51 / 422 (12.09%)	
occurrences (all)	126	95	
BLOOD AMYLASE INCREASED			
alternative dictionary used: CTCAE 3			

3		
subjects affected / exposed	4 / 411 (0.97%)	4 / 422 (0.95%)
occurrences (all)	4	5
BLOOD BILIRUBIN INCREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	18 / 411 (4.38%)	22 / 422 (5.21%)
occurrences (all)	40	37
BLOOD CREATINE PHOSPHOKINASE INCREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	2
BLOOD CREATININE INCREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	24 / 411 (5.84%)	33 / 422 (7.82%)
occurrences (all)	35	53
BLOOD HUMAN CHORIONIC GONADOTROPIN ABNORMAL		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
CD4 LYMPHOCYTES DECREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	13 / 411 (3.16%)	33 / 422 (7.82%)
occurrences (all)	25	96
COAGULOPATHY		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
GAMMA-GLUTAMYLTRANSFERASE INCREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	18 / 411 (4.38%)	19 / 422 (4.50%)
occurrences (all)	69	43
HAPTOGLOBIN		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	2
HYPERCHOLESTEROLAEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	7 / 411 (1.70%)	2 / 422 (0.47%)
occurrences (all)	8	6
INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
LEUKOPENIA NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	157 / 411 (38.20%)	191 / 422 (45.26%)
occurrences (all)	662	857
LIPASE INCREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	7 / 422 (1.66%)
occurrences (all)	1	17
LYMPHOPENIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	167 / 411 (40.63%)	179 / 422 (42.42%)
occurrences (all)	749	1113
METABOLIC/LABORATORY - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	39 / 411 (9.49%)	39 / 422 (9.24%)
occurrences (all)	130	159
NEUTROPHIL COUNT		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	97 / 411 (23.60%)	110 / 422 (26.07%)
occurrences (all)	263	298
PLATELET COUNT DECREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	169 / 411 (41.12%)	164 / 422 (38.86%)
occurrences (all)	579	533

<p>PROTHROMBIN TIME PROLONGED</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 411 (0.49%)</p> <p>2</p>	<p>7 / 422 (1.66%)</p> <p>31</p>	
<p>TROPONIN I INCREASED</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 411 (0.49%)</p> <p>2</p>	<p>0 / 422 (0.00%)</p> <p>0</p>	
<p>WEIGHT DECREASED</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>51 / 411 (12.41%)</p> <p>117</p>	<p>73 / 422 (17.30%)</p> <p>201</p>	
<p>WEIGHT INCREASED</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>18 / 411 (4.38%)</p> <p>41</p>	<p>14 / 422 (3.32%)</p> <p>18</p>	
<p>Injury, poisoning and procedural complications</p> <p>BURN:</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>CULTURE WOUND NEGATIVE</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>DERMATITIS RADIATION NOS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ECCHYMOSIS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>FRACTURE NOS</p> <p>alternative dictionary used: CTCAE</p>	<p>2 / 411 (0.49%)</p> <p>3</p> <p>2 / 411 (0.49%)</p> <p>2</p> <p>96 / 411 (23.36%)</p> <p>109</p> <p>12 / 411 (2.92%)</p> <p>23</p>	<p>1 / 422 (0.24%)</p> <p>1</p> <p>3 / 422 (0.71%)</p> <p>4</p> <p>103 / 422 (24.41%)</p> <p>121</p> <p>13 / 422 (3.08%)</p> <p>21</p>	

3			
subjects affected / exposed	4 / 411 (0.97%)	4 / 422 (0.95%)	
occurrences (all)	4	4	
INTRA-OPERATIVE INJURY: APPENDIX			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
INTRA-OPERATIVE INJURY: THORACIC DUCT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
RADIATION RECALL SYNDROME			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	20 / 411 (4.87%)	26 / 422 (6.16%)	
occurrences (all)	23	28	
VASCULAR ACCESS NOS COMPLICATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	7 / 411 (1.70%)	4 / 422 (0.95%)	
occurrences (all)	10	8	
VESSEL INJURY-ARTERY: OTHER NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
ANGINA PECTORIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences (all)	1	2	
ARRHYTHMIA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
ATRIAL FIBRILLATION			

alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	2 / 422 (0.47%)
occurrences (all)	5	3
ATRIAL TACHYCARDIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
CARDIAC GENERAL - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	3 / 422 (0.71%)
occurrences (all)	0	4
LEFT VENTRICULAR FAILURE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
MYOCARDIAL ISCHAEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
PALPITATIONS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	5 / 422 (1.18%)
occurrences (all)	5	6
SINUS BRADYCARDIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	2
SINUS TACHYCARDIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	6 / 422 (1.42%)
occurrences (all)	3	11
SUPRAVENTRICULAR EXTRASYSTOLES		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
SUPRAVENTRICULAR TACHYCARDIA alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
VENTRICULAR FIBRILLATION alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
VENTRICULAR TACHYCARDIA alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
ACCESSORY NERVE DISORDER NOS alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
ARACHNOIDITIS alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	2	
ATAXIA alternative dictionary used: CTCAE 3			
subjects affected / exposed	52 / 411 (12.65%)	56 / 422 (13.27%)	
occurrences (all)	95	114	
CEREBRAL ISCHAEMIA alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	6 / 422 (1.42%)	
occurrences (all)	7	6	
CEREBROSPINAL FLUID LEAK alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	3
CNS NECROSIS/CYSTIC PROGRESSION: alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)
occurrences (all)	6	3
COGNITIVE DISORDER alternative dictionary used: CTCAE 3		
subjects affected / exposed	31 / 411 (7.54%)	37 / 422 (8.77%)
occurrences (all)	60	62
CONVULSIONS NOS alternative dictionary used: CTCAE 3		
subjects affected / exposed	89 / 411 (21.65%)	98 / 422 (23.22%)
occurrences (all)	187	175
DEPRESSED LEVEL OF CONSCIOUSNESS alternative dictionary used: CTCAE 3		
subjects affected / exposed	17 / 411 (4.14%)	25 / 422 (5.92%)
occurrences (all)	23	33
DIZZINESS alternative dictionary used: CTCAE 3		
subjects affected / exposed	90 / 411 (21.90%)	75 / 422 (17.77%)
occurrences (all)	161	167
DYSGEUSIA alternative dictionary used: CTCAE 3		
subjects affected / exposed	43 / 411 (10.46%)	63 / 422 (14.93%)
occurrences (all)	90	126
ENCEPHALOPATHY alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	5 / 422 (1.18%)
occurrences (all)	2	5
EXTRAPYRAMIDAL DISORDER alternative dictionary used: CTCAE 3		

subjects affected / exposed	6 / 411 (1.46%)	7 / 422 (1.66%)
occurrences (all)	10	10
FACIAL NERVE DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	14 / 411 (3.41%)	12 / 422 (2.84%)
occurrences (all)	27	18
GLOSSOPHARYNGEAL NERVE DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	2	0
HEADACHE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	189 / 411 (45.99%)	197 / 422 (46.68%)
occurrences (all)	513	540
HEMORRHAGIC STROKE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	3 / 422 (0.71%)
occurrences (all)	1	3
HYDROCEPHALUS ACQUIRED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	4 / 422 (0.95%)
occurrences (all)	5	5
HYPERREFLEXIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	25 / 411 (6.08%)	23 / 422 (5.45%)
occurrences (all)	60	60
MEMORY IMPAIRMENT		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	79 / 411 (19.22%)	79 / 422 (18.72%)
occurrences (all)	196	183
MENTAL STATUS CHANGES		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	4 / 422 (0.95%)
occurrences (all)	11	6

MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): FACIAL		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	1 / 422 (0.24%)
occurrences (all)	8	1
NEURALGIA NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	3 / 422 (0.71%)
occurrences (all)	11	5
NEUROLOGY - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	32 / 411 (7.79%)	35 / 422 (8.29%)
occurrences (all)	55	57
NEUROPATHY: CRANIAL: CN VIII HEARING AND BALANCE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	7 / 411 (1.70%)	4 / 422 (0.95%)
occurrences (all)	16	13
NYSTAGMUS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	3 / 422 (0.71%)
occurrences (all)	2	4
OCULOMOTOR NERVE OPERATION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)
occurrences (all)	3	7
OLFACTORY NERVE DISORDER		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	2 / 422 (0.47%)
occurrences (all)	2	2
PERIPHERAL MOTOR NEUROPATHY		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	56 / 411 (13.63%)	65 / 422 (15.40%)
occurrences (all)	108	142
PERIPHERAL SENSORY NEUROPATHY		

alternative dictionary used: CTCAE 3		
subjects affected / exposed	56 / 411 (13.63%)	62 / 422 (14.69%)
occurrences (all)	103	165
RADICULITIS BRACHIAL		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	3	0
SINUS PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	3
SPEECH DISORDER		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	60 / 411 (14.60%)	60 / 422 (14.22%)
occurrences (all)	155	143
SYNCOPE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	6 / 422 (1.42%)
occurrences (all)	6	6
SYNCOPE VASOVAGAL		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)
occurrences (all)	3	1
TREMOR		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	51 / 411 (12.41%)	42 / 422 (9.95%)
occurrences (all)	93	122
TRIGEMINAL NERVE DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)
occurrences (all)	3	1
VITH NERVE DISORDER		
alternative dictionary used: CTCAE 3		

subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 4	1 / 422 (0.24%) 5	
Blood and lymphatic system disorders BLOOD/BONE MARROW - OTHER: alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	13 / 411 (3.16%) 51	13 / 422 (3.08%) 59	
BONE MARROW DEPRESSION NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	2 / 411 (0.49%) 2	0 / 422 (0.00%) 0	
FEBRILE NEUTROPENIA alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	3 / 411 (0.73%) 3	2 / 422 (0.47%) 2	
HAEMOLYSIS NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 1	1 / 422 (0.24%) 1	
HEMOGLOBIN alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	139 / 411 (33.82%) 505	173 / 422 (41.00%) 581	
LYMPHATICS - OTHER: alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	2 / 411 (0.49%) 4	3 / 422 (0.71%) 3	
SPLEEN DISORDER NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 6	1 / 422 (0.24%) 1	
THROMBOTIC MICROANGIOPATHY NOS alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
AUDITORY/EAR - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	14 / 411 (3.41%)	11 / 422 (2.61%)	
occurrences (all)	24	18	
EAR PAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	8 / 422 (1.90%)	
occurrences (all)	7	12	
HEARING DISABILITY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences (all)	0	2	
HEARING IMPAIRED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	26 / 411 (6.33%)	19 / 422 (4.50%)	
occurrences (all)	69	37	
OTITIS EXTERNA NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	8 / 411 (1.95%)	10 / 422 (2.37%)	
occurrences (all)	15	16	
OTITIS MEDIA SEROUS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	7 / 422 (1.66%)	
occurrences (all)	3	11	
PAIN: EXTERNAL EAR			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences (all)	2	2	
TINNITUS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	12 / 411 (2.92%)	11 / 422 (2.61%)	
occurrences (all)	23	18	
Eye disorders			
CATARACT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	4 / 422 (0.95%)	
occurrences (all)	1	11	
CONJUNCTIVITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)	
occurrences (all)	2	1	
DIPLOPIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	10 / 411 (2.43%)	8 / 422 (1.90%)	
occurrences (all)	38	20	
DRY EYE NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 411 (0.73%)	9 / 422 (2.13%)	
occurrences (all)	4	13	
EXTRAOCULAR MUSCLE DISORDER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	4 / 422 (0.95%)	
occurrences (all)	6	4	
EYE PAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 411 (0.97%)	8 / 422 (1.90%)	
occurrences (all)	5	14	
EYELID FUNCTION DISORDER NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	5 / 422 (1.18%)	
occurrences (all)	1	10	
GLAUCOMA NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
LACRIMATION INCREASED		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	6 / 411 (1.46%)	11 / 422 (2.61%)
occurrences (all)	8	21
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): OCULAR		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	2	0
OCULAR/VISUAL - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	35 / 411 (8.52%)	27 / 422 (6.40%)
occurrences (all)	78	67
OPTIC DISC DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	2 / 422 (0.47%)
occurrences (all)	8	3
OPTIC NERVE DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	13 / 411 (3.16%)	12 / 422 (2.84%)
occurrences (all)	31	18
PHOTOPHOBIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	6 / 422 (1.42%)
occurrences (all)	4	10
PHOTOPSIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	6 / 411 (1.46%)	3 / 422 (0.71%)
occurrences (all)	14	4
PROPTOSIS		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	2 / 411 (0.49%)	2 / 422 (0.47%)	
occurrences (all)	2	4	
RETINAL DETACHMENT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	4	0	
UVEITIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
VISION BLURRED			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	44 / 411 (10.71%)	54 / 422 (12.80%)	
occurrences (all)	98	110	
Gastrointestinal disorders			
ABDOMINAL DISTENTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)	
occurrences (all)	4	6	
ABDOMINAL PAIN NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	17 / 411 (4.14%)	25 / 422 (5.92%)	
occurrences (all)	24	37	
ANAL DISCOMFORT			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
ANAL HAEMORRHAGE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
COLITIS NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	2	0
COLONIC PERFORATION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	2
CONSTIPATION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	134 / 411 (32.60%)	127 / 422 (30.09%)
occurrences (all)	297	336
DIARRHOEA NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	48 / 411 (11.68%)	74 / 422 (17.54%)
occurrences (all)	73	127
DRY MOUTH		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	22 / 411 (5.35%)	26 / 422 (6.16%)
occurrences (all)	36	56
DYSPEPSIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	30 / 411 (7.30%)	30 / 422 (7.11%)
occurrences (all)	43	39
DYSPHAGIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	9 / 411 (2.19%)	14 / 422 (3.32%)
occurrences (all)	10	19
ENTERITIS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
ESOPHAGEAL PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1

ESOPHAGEAL ULCER		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
FAECAL INCONTINENCE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	7 / 422 (1.66%)
occurrences (all)	5	9
FLATULENCE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	5 / 422 (1.18%)
occurrences (all)	2	5
GASTRIC ULCER		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	3	0
GASTRITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	4 / 422 (0.95%)
occurrences (all)	1	4
GASTROINTESTINAL - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	12 / 411 (2.92%)	9 / 422 (2.13%)
occurrences (all)	17	23
GASTROINTESTINAL PAIN NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	3 / 422 (0.71%)
occurrences (all)	0	10
HEMORRHOIDS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	2 / 422 (0.47%)
occurrences (all)	6	2
ILEUS PARALYTIC		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
LIP PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
LOWER GASTROINTESTINAL HEMORRHAGE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	2	0
MOUTH HAEMORRHAGE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	2	0
MUCOSITIS/STOMATITIS (CLINICAL EXAM): ANUS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	2
NAUSEA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	225 / 411 (54.74%)	228 / 422 (54.03%)
occurrences (all)	517	598
ORAL PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	4 / 422 (0.95%)
occurrences (all)	4	4
OSEOPHAGITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)
occurrences (all)	2	1
PAIN: PERITONEUM		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
PANCREATIC HEMORRHAGE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
PANCREATITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
PERIDONTAL DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	2	7
PROCTALGIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	3
RADIATION MUCOSITIS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	5 / 422 (1.18%)
occurrences (all)	4	7
RECTAL HEMORRHAGE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)
occurrences (all)	5	3
SALIVARY GLAND DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	0 / 422 (0.00%)
occurrences (all)	3	0
STOMACH DISCOMFORT		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	2 / 422 (0.47%)
occurrences (all)	5	2

<p>STOMATITIS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>19 / 411 (4.62%)</p> <p>20</p>	<p>24 / 422 (5.69%)</p> <p>33</p>	
<p>STRICTURE/STENOSIS (INCLUDING ANASTOMOTIC), GI: PANCREAS/PANCREATIC DUCT</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 411 (0.24%)</p> <p>2</p>	<p>0 / 422 (0.00%)</p> <p>0</p>	
<p>TOOTH DISORDER NOS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 411 (0.24%)</p> <p>6</p>	<p>0 / 422 (0.00%)</p> <p>0</p>	
<p>TOOTHACHE</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 411 (0.73%)</p> <p>3</p>	<p>1 / 422 (0.24%)</p> <p>1</p>	
<p>VOMITING NOS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>114 / 411 (27.74%)</p> <p>190</p>	<p>120 / 422 (28.44%)</p> <p>207</p>	
<p>Hepatobiliary disorders</p> <p>CHOLECYSTITIS NOS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 411 (0.49%)</p> <p>4</p>	<p>1 / 422 (0.24%)</p> <p>1</p>	
<p>GALLBLADDER PAIN</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 411 (0.49%)</p> <p>2</p>	<p>1 / 422 (0.24%)</p> <p>1</p>	
<p>HEPATIC FAILURE</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 411 (0.24%)</p> <p>1</p>	<p>0 / 422 (0.00%)</p> <p>0</p>	
<p>HEPATOBIILIARY/PANCREAS - OTHER:</p>			

alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
ACNE NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	8 / 411 (1.95%)	7 / 422 (1.66%)	
occurrences (all)	11	8	
ALOPECIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	172 / 411 (41.85%)	190 / 422 (45.02%)	
occurrences (all)	437	515	
DECUBITUS ULCER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)	
occurrences (all)	1	2	
DERMATITIS EXFOLIATIVE NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	63 / 411 (15.33%)	77 / 422 (18.25%)	
occurrences (all)	109	128	
DERMATOLOGY/SKIN - OTHER:			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	15 / 411 (3.65%)	18 / 422 (4.27%)	
occurrences (all)	17	31	
DRY SKIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	19 / 411 (4.62%)	17 / 422 (4.03%)	
occurrences (all)	51	24	
ERYTHEMA MULTIFORME			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 411 (1.22%)	6 / 422 (1.42%)	
occurrences (all)	5	7	
FAT ATROPHY NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	2
LOCALISED EXFOLIATION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	3 / 422 (0.71%)
occurrences (all)	4	4
NAIL DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	2 / 422 (0.47%)
occurrences (all)	12	5
PAIN OF SKIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	4 / 422 (0.95%)
occurrences (all)	4	5
PAIN: SCALP		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	4 / 422 (0.95%)
occurrences (all)	8	5
PETECHIAE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	7 / 411 (1.70%)	2 / 422 (0.47%)
occurrences (all)	8	4
PHOTOSENSITIVITY REACTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	2 / 422 (0.47%)
occurrences (all)	4	2
PRURITUS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	43 / 411 (10.46%)	53 / 422 (12.56%)
occurrences (all)	81	71
SKIN HYPERPIGMENTATION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	10 / 411 (2.43%)	10 / 422 (2.37%)
occurrences (all)	17	16

<p>SKIN HYPOPIGMENTATION</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 411 (0.00%)</p> <p>0</p>	<p>2 / 422 (0.47%)</p> <p>5</p>	
<p>SWEATING INCREASED</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>7 / 411 (1.70%)</p> <p>14</p>	<p>4 / 422 (0.95%)</p> <p>8</p>	
<p>ULCERATION:</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 411 (0.73%)</p> <p>3</p>	<p>2 / 422 (0.47%)</p> <p>5</p>	
<p>URTICARIA NOS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 411 (0.73%)</p> <p>3</p>	<p>3 / 422 (0.71%)</p> <p>4</p>	
<p>Renal and urinary disorders</p> <p>BLADDER PAIN</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 411 (0.00%)</p> <p>0</p>	<p>1 / 422 (0.24%)</p> <p>1</p>	
<p>BLADDER SPASM</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 411 (0.24%)</p> <p>1</p>	<p>1 / 422 (0.24%)</p> <p>1</p>	
<p>CHROMATURIA</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 411 (0.00%)</p> <p>0</p>	<p>3 / 422 (0.71%)</p> <p>3</p>	
<p>CYSTITIS NOS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 411 (0.49%)</p> <p>2</p>	<p>6 / 422 (1.42%)</p> <p>8</p>	
<p>GLOMERULAR FILTRATION RATE</p> <p>alternative dictionary used: CTCAE 3</p>			

subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)
occurrences (all)	8	3
HEMOGLOBINURIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)
occurrences (all)	11	3
PERFORATION, GU: SPERMATIC CORD		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
POLLAKIURIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	20 / 411 (4.87%)	20 / 422 (4.74%)
occurrences (all)	30	41
PROTEINURIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	3 / 422 (0.71%)
occurrences (all)	3	3
RENAL FAILURE NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	3 / 422 (0.71%)
occurrences (all)	1	3
RENAL/GENITOURINARY - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	4 / 422 (0.95%)
occurrences (all)	3	5
URETERIC OBSTRUCTION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
URETHRAL OBSTRUCTION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1

<p>URINARY BLADDER HEMORRHAGE</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>URINARY INCONTINENCE</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>URINARY RETENTION</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>UROGENITAL HEMORRHAGE</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>			
	1 / 411 (0.24%)	0 / 422 (0.00%)	
	1	0	
	14 / 411 (3.41%)	22 / 422 (5.21%)	
	22	36	
	6 / 411 (1.46%)	3 / 422 (0.71%)	
	8	4	
	1 / 411 (0.24%)	1 / 422 (0.24%)	
	1	1	
<p>Endocrine disorders</p> <p>CUSHINGOID</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ENDOCRINE - OTHER:</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>HYPOTHYROIDISM</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>THYROTOXICOSIS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>			
	15 / 411 (3.65%)	13 / 422 (3.08%)	
	28	26	
	2 / 411 (0.49%)	5 / 422 (1.18%)	
	2	13	
	1 / 411 (0.24%)	0 / 422 (0.00%)	
	1	0	
	0 / 411 (0.00%)	1 / 422 (0.24%)	
	0	1	
Musculoskeletal and connective tissue disorders			

ARTHRALGIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	26 / 411 (6.33%)	30 / 422 (7.11%)
occurrences (all)	78	80
ARTHRITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	3 / 422 (0.71%)
occurrences (all)	2	4
BACK PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	22 / 411 (5.35%)	24 / 422 (5.69%)
occurrences (all)	59	38
BONE PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	5 / 422 (1.18%)
occurrences (all)	6	8
BUTTOCK PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
CHEST WALL PAIN		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	5 / 422 (1.18%)
occurrences (all)	1	5
EXTREMITY-UPPER (FUNCTION):		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	1 / 422 (0.24%)
occurrences (all)	3	1
JOINT DISORDER NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	3 / 422 (0.71%)
occurrences (all)	13	9
MUSCLE WEAKNESS NOS		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	40 / 411 (9.73%)	51 / 422 (12.09%)
occurrences (all)	76	98
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): EXTREMITY-LOWER alternative dictionary used: CTCAE 3		
subjects affected / exposed	31 / 411 (7.54%)	25 / 422 (5.92%)
occurrences (all)	55	50
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): EXTREMITY-UPPER alternative dictionary used: CTCAE 3		
subjects affected / exposed	17 / 411 (4.14%)	10 / 422 (2.37%)
occurrences (all)	29	17
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): LEFT-SIDED alternative dictionary used: CTCAE 3		
subjects affected / exposed	21 / 411 (5.11%)	16 / 422 (3.79%)
occurrences (all)	64	33
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): RIGHT-SIDED alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	8 / 422 (1.90%)
occurrences (all)	5	11
MUSCLE WEAKNESS, GENERALIZED OR SPECIFIC AREA (NOT DUE TO NEUROPATHY): TRUNK alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
MUSCULOSKELETAL/SOFT TISSUE - OTHER: alternative dictionary used: CTCAE 3		
subjects affected / exposed	13 / 411 (3.16%)	14 / 422 (3.32%)
occurrences (all)	24	29
MYALGIA alternative dictionary used: CTCAE 3		

subjects affected / exposed	13 / 411 (3.16%)	22 / 422 (5.21%)	
occurrences (all)	25	45	
NECK PAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	12 / 411 (2.92%)	9 / 422 (2.13%)	
occurrences (all)	20	11	
OSTEOPOROSIS NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
PAIN IN EXTREMITY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	23 / 411 (5.60%)	31 / 422 (7.35%)	
occurrences (all)	44	47	
SOFT TISSUE NECROSIS: HEAD			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)	
occurrences (all)	1	0	
TRISMUS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences (all)	1	1	
Infections and infestations			
ABDOMINAL INFECTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)	
occurrences (all)	1	1	
ADENOVIRAL HEPATITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)	
occurrences (all)	0	1	
BLADDER INFECTION NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 411 (0.49%)	6 / 422 (1.42%)
occurrences (all)	2	6
ANO-RECTAL INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	2
BONE INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	3	0
BRONCHITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	6 / 422 (1.42%)
occurrences (all)	2	6
CLOSTRIDIAL INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
EAR INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
ENCEPHALITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
EYE INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	5 / 422 (1.18%)
occurrences (all)	1	5
GENITAL INFECTION NOS, FEMALE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1

GINGIVAL INFECTION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	7 / 411 (1.70%)	3 / 422 (0.71%)
occurrences (all)	9	4
INFECTION - OTHER:		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	17 / 411 (4.14%)	17 / 422 (4.03%)
occurrences (all)	22	25
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): BILIARY TREE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): BLADDER (URINARY)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	2
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): BRAIN (ENCEPHALITIS, INFECTIOUS)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): EXTERNAL EAR (OTITIS EXTERNA)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): GALLBLADDER (CHOLECYSTITIS)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L):		

KIDNEY		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): LUNG (PNEUMONIA)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	6 / 422 (1.42%)
occurrences (all)	2	12
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): NOSE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): ORAL CAVITY-GUMS (GINGIVITIS)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	2
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): PARANASAL		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): RECTUM		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): SOFT TISSUE NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L):		

UPPER AIRWAY NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	2	0
INFECTION WITH GRADE 3 OR 4 NEUTROPHILS (ANC <1.0 X 10E9/L): URINARY TRACT NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	4
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: APPENDIX		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: ARTERY		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: BLOOD		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	3
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: COLON		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: CONJUNCTIVA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS:		

ESOPHAGUS

alternative dictionary used: CTCAE 3

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: EXTERNAL EAR (OTITIS EXTERNA)

alternative dictionary used: CTCAE 3

subjects affected / exposed	3 / 411 (0.73%)	0 / 422 (0.00%)
occurrences (all)	3	0

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: LIP/PERIORAL

alternative dictionary used: CTCAE 3

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: NERVE-PERIPHERAL

alternative dictionary used: CTCAE 3

subjects affected / exposed	2 / 411 (0.49%)	0 / 422 (0.00%)
occurrences (all)	2	0

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: PARANASAL

alternative dictionary used: CTCAE 3

subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: UPPER AERODIGESTIVE NOS

alternative dictionary used: CTCAE 3

subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0

INFECTION WITH NORMAL ANC OR GRADE 1 OR 2 NEUTROPHILS: WOUND

alternative dictionary used: CTCAE 3

subjects affected / exposed	4 / 411 (0.97%)	4 / 422 (0.95%)
occurrences (all)	4	6

INFECTION WITH UNKNOWN ANC: BLADDER (URINARY)

alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
INFECTION WITH UNKNOWN ANC: BRAIN (ENCEPHALITIS, INFECTIOUS)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
INFECTION WITH UNKNOWN ANC: LIP/PERIORAL		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
INFECTION WITH UNKNOWN ANC: LUNG (PNEUMONIA)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	1
INFECTION WITH UNKNOWN ANC: ORAL CAVITY-GUMS (GINGIVITIS)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	2
INFECTION WITH UNKNOWN ANC: SINUS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	2
INFECTION WITH UNKNOWN ANC: SKIN (CELLULITIS)		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	0 / 422 (0.00%)
occurrences (all)	3	0
INFECTION WITH UNKNOWN ANC: UNGUAL (NAILS)		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	2
INFECTION WITH UNKNOWN ANC: URINARY TRACT NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	3 / 411 (0.73%)	2 / 422 (0.47%)
occurrences (all)	3	2
INFECTIOUS MENINGITIS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	1 / 422 (0.24%)
occurrences (all)	1	2
NASOPHARYNGITIS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	2 / 422 (0.47%)
occurrences (all)	0	3
OPPORTUNISITIC INFECTION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	6 / 411 (1.46%)	9 / 422 (2.13%)
occurrences (all)	9	13
OTITIS MEDIA NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	2
PHARYNGITIS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	3 / 422 (0.71%)
occurrences (all)	1	3
PNEUMONIA NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	5 / 411 (1.22%)	9 / 422 (2.13%)
occurrences (all)	5	10
RESPIRATORY TRACT INFECTION NOS		
alternative dictionary used: CTCAE 3		

subjects affected / exposed	8 / 411 (1.95%)	18 / 422 (4.27%)
occurrences (all)	10	22
RHINITIS INFECTIVE		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	2 / 422 (0.47%)
occurrences (all)	6	2
SEPSIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1
SINUSITIS NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	5 / 422 (1.18%)
occurrences (all)	1	7
SKIN INFECTION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	8 / 411 (1.95%)	9 / 422 (2.13%)
occurrences (all)	8	11
SOFT TISSUE INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	0 / 422 (0.00%)
occurrences (all)	1	0
TOOTH INFECTION		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	1 / 411 (0.24%)	2 / 422 (0.47%)
occurrences (all)	1	2
URINARY TRACT INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	7 / 422 (1.66%)
occurrences (all)	4	8
VAGINAL INFECTION NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	0 / 411 (0.00%)	1 / 422 (0.24%)
occurrences (all)	0	1

WOUND INFECTION alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	2 / 411 (0.49%) 2	4 / 422 (0.95%) 7	
Metabolism and nutrition disorders			
ACIDOSIS NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 1	1 / 422 (0.24%) 1	
ALKALOSIS NOS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	1 / 411 (0.24%) 1	0 / 422 (0.00%) 0	
ANOREXIA alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	114 / 411 (27.74%) 210	141 / 422 (33.41%) 328	
BLOOD BICARBONATE DECREASED alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	7 / 411 (1.70%) 14	6 / 422 (1.42%) 9	
DEHYDRATION alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	18 / 411 (4.38%) 21	19 / 422 (4.50%) 25	
GLUCOSE TOLERANCE IMPAIRED alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	0 / 411 (0.00%) 0	1 / 422 (0.24%) 1	
HYPERCALCAEMIA alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all)	2 / 411 (0.49%) 3	10 / 422 (2.37%) 11	
HYPERGLYCAEMIA NOS alternative dictionary used: CTCAE 3			

subjects affected / exposed	120 / 411 (29.20%)	128 / 422 (30.33%)
occurrences (all)	349	311
HYPERKALAEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	16 / 411 (3.89%)	15 / 422 (3.55%)
occurrences (all)	21	19
HYPERMAGNESAEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	2 / 422 (0.47%)
occurrences (all)	4	3
HYPERNATREMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	21 / 411 (5.11%)	20 / 422 (4.74%)
occurrences (all)	30	32
HYPERTRIGLYCERIDAEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	2 / 411 (0.49%)	1 / 422 (0.24%)
occurrences (all)	2	1
HYPERURICEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	4 / 411 (0.97%)	8 / 422 (1.90%)
occurrences (all)	7	15
HYPOALBUMINEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	45 / 411 (10.95%)	59 / 422 (13.98%)
occurrences (all)	83	115
HYPOCALCEMIA		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	38 / 411 (9.25%)	44 / 422 (10.43%)
occurrences (all)	55	63
HYPOGLYCEMIA NOS		
alternative dictionary used: CTCAE 3		
subjects affected / exposed	22 / 411 (5.35%)	21 / 422 (4.98%)
occurrences (all)	30	34

HYPOKALEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	46 / 411 (11.19%)	55 / 422 (13.03%)	
occurrences (all)	90	87	
HYPOMAGNESEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	6 / 411 (1.46%)	4 / 422 (0.95%)	
occurrences (all)	7	6	
HYPONATREMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	49 / 411 (11.92%)	61 / 422 (14.45%)	
occurrences (all)	84	109	
HYPOPHOSPHATAEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	7 / 411 (1.70%)	7 / 422 (1.66%)	
occurrences (all)	12	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported