



## Clinical trial results:

### Phase III trial exploring the combination of bevacizumab and lomustine in patients with first recurrence of a glioblastoma.

#### Summary

EudraCT number	2010-023218-30
Trial protocol	BE NL AT IT
Global end of trial date	10 February 2018

#### Results information

Result version number	v1 (current)
This version publication date	29 March 2019
First version publication date	29 March 2019

#### Trial information

##### Trial identification

Sponsor protocol code	26101
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01290939
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	EORTC
Sponsor organisation address	83 Avenue Mounier, Brussels, Belgium, 1200
Public contact	Project-Budget & Regulatory Dept, EORTC, 0032 27741047/, regulatory@eortc.be
Scientific contact	Project-Budget & Regulatory Dept, EORTC, 0032 27741047/, regulatory@eortc.be

Notes:

#### Paediatric regulatory details

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

Notes:

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## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2015
Global end of trial reached?	Yes
Global end of trial date	10 February 2018
Was the trial ended prematurely?	No

Notes:

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## General information about the trial

Main objective of the trial:

The primary objective of this study is to investigate whether the addition of bevacizumab to lomustine improves overall survival (OS) in patients with recurrent glioblastoma compared to treatment with lomustine alone.

Protection of trial subjects:

The responsible investigator ensured that this study was conducted in agreement with either the Declaration of Helsinki (available on the World Medical Association web site (<http://www.wma.net>)) and/or the laws and regulations of the country, whichever provides the greatest protection of the patient. The protocol was written, and the study conducted according to the ICH Harmonized Tripartite Guideline on Good Clinical Practice (ICH-GCP, available online at [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/09/WC500002874.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002874.pdf)).

The protocol was approved by the competent ethics committee(s) as required by the applicable national legislation.

Safety data were reviewed within the EORTC Headquarters on a regular basis as part of the Medical Review process. Problems which were identified were discussed with the Study Coordinators who took appropriate measures. Safety information were also included in trial status reports which served as a basis of discussion during EORTC Group meetings. These reports were made available to investigators

Background therapy:

Procarbazine and nitrosoureas are modestly effective as systemic agents, although they were evaluated much before temozolomide and rigorous trials meeting current standards are absent. Concomitant and adjuvant temozolomide to radiotherapy is now the standard of care in newly diagnosed patients; however its use at the time of recurrence is debatable and in this setting nitrosoureas are currently widely used, in particular Lomustine (CCNU). A recent randomized study on recurrent glioblastoma that used lomustine noted a 19% progression free survival probability at 6 months with lomustine, similar to what had previously been observed with temozolomide in this indication. Further lomustine was used as comparator in most current trials. The REGAL trial aiming at proving superiority of a vascular endothelial receptor 2 antagonist (cediranib) alone or in combination with lomustine over lomustine alone was negative as reported at a scientific meeting. However, all data presented so far also spoke for relevant activity of lomustine in this trial, and this drug was currently widely used as a salvage regimen for recurrent glioblastoma, despite its modest activity.

Evidence for comparator:

In recent years studies on anti-angiogenic agents received considerable attention because of high response rates. Trials on the above mentioned tyrosine kinase inhibitor cediranib and the humanized monoclonal antibody against circulating VEGF bevacizumab had attracted the most interest. Until now phase II trials with anti-angiogenic agents had provided promising results that required confirmation in larger and, even more important, controlled trials. Indeed, the randomized REGAL trial failed to provide evidence of better outcome in cediranib treated recurrent glioblastoma patients, despite high response rates in uncontrolled phase II studies. For bevacizumab, the promising activity observed in recurrent glioblastoma remained to be confirmed, despite the large number of uncontrolled phase II trials that had been conducted. In particular properly powered studies showing Overall Survival benefit from bevacizumab in recurrent glioblastoma were still lacking. Indeed, all but one study on bevacizumab in recurrent glioma were uncontrolled phase II studies. As of today only one randomized, non-comparative phase II study has been reported, but with an irrelevant control. This randomized phase II study observed a PFS6 of 43% after beva given as single agent and of 50% if given in combination with irinotecan. OS was very similar in both groups (approximately 9 months). Compared to the usually less than 10% obtained in recurrent glioblastoma, the observed response rates were exceptionally high (40-45% as judged by the local investigators, 28-38% after central review), and PFS6 (the agreed upon

endpoint in trials on recurrent glioblastoma) was twice as high compared to trials on temozolomide and nitrosoureas. Based on the high response rates observed in this trial, in the US bevacizumab had been conditionally approved for use in recurrent glioblastoma. The registration application of bevacizumab in Europe had been denied, because of lack appropriately controlled trials.

Actual start date of recruitment	21 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 124
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 39
Country: Number of subjects enrolled	France: 106
Country: Number of subjects enrolled	Germany: 74
Country: Number of subjects enrolled	Italy: 63
Country: Number of subjects enrolled	Switzerland: 12
Worldwide total number of subjects	437
EEA total number of subjects	425

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)	327
From 65 to 84 years	110
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Four hundred forty seven patients were randomized by 38 institutions in 8 countries (AT, BE, FR, DE, IT, CH, NL, UK). They were recruited between 21/11/2011 and 23/12/2014. The average monthly recruitment rate was 12 pts/mo and 27 pts/mo during the last 6 months.

### Pre-assignment

Screening details:

There was no screening period. Eligible patients were randomized to either LOM or LOM+Bv

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Arm1: LOM+Bv

Arm description:

Lomustine 90 mg/m<sup>2</sup> every 6 weeks (cap. 160 mg) + bevacizumab 10 mg/kg every 2 weeks until one of the withdrawal criteria have been met (followed by best investigators choice at further progression). In the absence of hematological toxicity > grade 1 during the first cycle the dose of lomustine can be escalated to 110 mg/m<sup>2</sup> (cap 200 mg) in their second cycle.

Arm type	Experimental
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Bevacizumab 10 mg/kg every 2 weeks (at further progression treatment will be according to investigators discretion). In the absence of hematological toxicity > grade 1 during the first cycle the dose of lomustine can be escalated to 110 mg/m<sup>2</sup> (cap 200 mg) in their second cycle.

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

Dosage and administration details:

Lomustine 90 mg/m<sup>2</sup> orally on day 1 every 6 weeks (cap. 160 mg) In the absence of hematological toxicity > grade 1 during the first cycle the dose of lomustine can be escalated to 110 mg/m<sup>2</sup> (cap 200 mg) in their second cycle. Lomustine treatment will be repeated every six weeks.

<b>Arm title</b>	Arm 2: LOM
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Arm description:

Arm 2: Lomustine

Arm type	Active comparator
Investigational medicinal product name	Lomustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

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**Dosage and administration details:**

Arm 2: Lomustine 110 mg/m<sup>2</sup> orally on day 1 every 6 weeks (cap at 200mg). Lomustine will be repeated every six weeks.

<b>Number of subjects in period 1</b>	Arm1: LOM+Bv	Arm 2: LOM
Started	288	149
Completed	264	144
Not completed	24	5
Treatment ongoing at time of database lock	24	-
Ongoing treatment at time of database lock	-	5

## Baseline characteristics

### Reporting groups

Reporting group title	Arm1: LOM+Bv
Reporting group description: Lomustine 90 mg/m <sup>2</sup> every 6 weeks (cap. 160 mg) + bevacizumab 10 mg/kg every 2 weeks until one of the withdrawal criteria have been met (followed by best investigators choice at further progression). In the absence of hematological toxicity > grade 1 during the first cycle the dose of lomustine can be escalated to 110 mg/m <sup>2</sup> (cap 200 mg) in their second cycle.	
Reporting group title	Arm 2: LOM
Reporting group description: Arm 2: Lomustine	

Reporting group values	Arm1: LOM+Bv	Arm 2: LOM	Total
Number of subjects	288	149	437
Age categorical			
Age at randomization			
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)	218	109	327
From 65-84 years	70	40	110
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	114	58	172
Male	174	91	265

### Subject analysis sets

Subject analysis set title	Intent-to-Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized patients will be analyzed in the arm they were allocated by randomization.	

Reporting group values	Intent-to-Treat		
Number of subjects	437		
Age categorical			
Age at randomization			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	327		
From 65-84 years	110		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	172		
Male	265		

## End points

### End points reporting groups

Reporting group title	Arm1: LOM+Bv
Reporting group description: Lomustine 90 mg/m <sup>2</sup> every 6 weeks (cap. 160 mg) + bevacizumab 10 mg/kg every 2 weeks until one of the withdrawal criteria have been met (followed by best investigators choice at further progression). In the absence of hematological toxicity > grade 1 during the first cycle the dose of lomustine can be escalated to 110 mg/m <sup>2</sup> (cap 200 mg) in their second cycle.	
Reporting group title	Arm 2: LOM
Reporting group description: Arm 2: Lomustine	
Subject analysis set title	Intent-to-Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized patients will be analyzed in the arm they were allocated by randomization.	

### Primary: Overall Survival

End point title	Overall Survival
End point description:	
End point type	Primary
End point timeframe: Overall Survival (OS) is calculated from the date of randomization up to the date of death (any cause). For patients still alive or lost to follow-up at the time of analysis, OS will be censored at last follow-up visit date.	

End point values	Arm1: LOM+Bv	Arm 2: LOM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	149		
Units: Months				
median (confidence interval 95%)	9.1 (8.1 to 10.1)	8.6 (7.6 to 10.4)		

### Statistical analyses

Statistical analysis title	Primary analysis of OS
Statistical analysis description: For the primary analysis of OS, the stratified Log-rank test will be computed and the Cox proportional hazards model will be fitted with the treatment (LOM+Bv compared to LOM) stratified by the stratification factors at randomization ( WHO PS: 0 vs >0, Steroids administration Y/N, Largest diameter of tumor ≤40mm vs >40mm but not institution) and by a variable indicating if the patient was recruited in the phase II or in the phase III.	
Comparison groups	Arm1: LOM+Bv v Arm 2: LOM

Number of subjects included in analysis	437
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.65
Method	Stratified logrank test

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Before treatment start, From treatment start until end of study treatment Every 2 weeks , Every 6 weeks (day 42 of each cycle), From end of study treatment until progressive disease Every 12 weeks, From disease progression until death Every 12 weeks.

Adverse event reporting additional description:

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

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18
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### Reporting groups

Reporting group title	Arm 2: LOM
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Reporting group description:

Lomustine

Reporting group title	Arm 1 : LOM+Bv
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Reporting group description:

Lomustine+Bevacizumab

Serious adverse events	Arm 2: LOM	Arm 1 : LOM+Bv	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 147 (19.05%)	87 / 283 (30.74%)	
number of deaths (all causes)	112	213	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL ADENOCARCINOMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRADUCTAL PROLIFERATIVE BREAST LESION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

DEEP VEIN THROMBOSIS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0	1 / 283 (0.35%) 1 / 1 0 / 0	
HYPERTENSION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0	1 / 283 (0.35%) 1 / 1 0 / 0	
NECROSIS ISCHAEMIC alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0	1 / 283 (0.35%) 1 / 1 0 / 0	
General disorders and administration site conditions FATIGUE alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0	2 / 283 (0.71%) 1 / 2 0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 147 (0.68%) 1 / 1 0 / 0	1 / 283 (0.35%) 0 / 1 0 / 0	
OEDEMA PERIPHERAL alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 147 (0.68%) 0 / 1 0 / 0	0 / 283 (0.00%) 0 / 0 0 / 0	
PYREXIA alternative dictionary used:			

MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
DYSпноEA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	15 / 283 (5.30%)	
occurrences causally related to treatment / all	0 / 2	15 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISORDER			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
DISORIENTATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPARTATE AMINOTRANSFERASE INCREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATINE PHOSPHOKINASE INCREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			

alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
BRAIN CONTUSION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CRANIOCEREBRAL INJURY			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
FALL			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBAR VERTEBRAL FRACTURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOCEPHALUS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND COMPLICATION			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND DEHISCENCE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CARDIAC FAILURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE CONGESTIVE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR FAILURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
BRAIN OEDEMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL ISCHAEMIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COGNITIVE DISORDER			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS POSTURAL			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSAESTHESIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPILEPSY			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FOCAL DYSCOGNITIVE SEIZURES			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERALISED TONIC-CLONIC SEIZURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGE INTRACRANIAL			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPARESIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROLOGICAL DECOMPENSATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARTIAL SEIZURES			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
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: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTICTAL STATE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	13 / 283 (4.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	

SIMPLE PARTIAL SEIZURES alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 147 (0.68%) 0 / 1 0 / 0	0 / 283 (0.00%) 0 / 0 0 / 0	
SOMNOLENCE alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 147 (0.68%) 0 / 1 0 / 0	0 / 283 (0.00%) 0 / 0 0 / 0	
SPEECH DISORDER alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 147 (0.68%) 0 / 1 0 / 0	1 / 283 (0.35%) 0 / 1 0 / 0	
STATUS EPILEPTICUS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 147 (0.68%) 0 / 1 0 / 0	1 / 283 (0.35%) 0 / 1 0 / 0	
SYNCOPE alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0	2 / 283 (0.71%) 0 / 2 0 / 0	
TRANSIENT ISCHAEMIC ATTACK alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0	1 / 283 (0.35%) 0 / 1 0 / 0	
Blood and lymphatic system disorders ANAEMIA alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHOPENIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 147 (2.04%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	7 / 147 (4.76%)	12 / 283 (4.24%)	
occurrences causally related to treatment / all	8 / 8	11 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
BLINDNESS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RETINOPATHY			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal disorders</b>			
<b>ABDOMINAL PAIN</b>			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>COLITIS</b>			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>COLITIS EROSIVE</b>			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>CONSTIPATION</b>			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>DUODENAL ULCER HAEMORRHAGE</b>			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>DYSPHAGIA</b>			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL PERFORATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHOIDAL HAEMORRHAGE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INGUINAL HERNIA STRANGULATED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINE PERFORATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
NAUSEA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

<b>PERITONEAL NECROSIS</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 147 (0.00%)  0 / 0  0 / 0	  1 / 283 (0.35%)  1 / 1  0 / 0	
<b>RECTAL HAEMORRHAGE</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 147 (0.00%)  0 / 0  0 / 0	  1 / 283 (0.35%)  1 / 1  0 / 0	
<b>VOMITING</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 147 (0.00%)  0 / 0  0 / 0	  1 / 283 (0.35%)  1 / 1  0 / 0	
<b>Hepatobiliary disorders</b> <b>PORTAL HYPERTENSION</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 147 (0.00%)  0 / 0  0 / 0	  1 / 283 (0.35%)  1 / 1  0 / 0	
<b>Renal and urinary disorders</b> <b>PROTEINURIA</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 147 (0.00%)  0 / 0  0 / 0	  1 / 283 (0.35%)  1 / 1  0 / 0	
<b>RENAL FAILURE</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 147 (0.00%)  0 / 0  0 / 0	  1 / 283 (0.35%)  1 / 1  0 / 0	
<b>RENAL MASS</b> alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY BLADDER HAEMORRHAGE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
STEROID WITHDRAWAL SYNDROME			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
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			
ARTHRALGIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABSCCESS SOFT TISSUE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL ABSCESS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYSTITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED SEPSIS			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS VIRAL			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL VIRAL INFECTION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	4 / 283 (1.41%)	
occurrences causally related to treatment / all	2 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PNEUMOCOCCAL			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTOPERATIVE WOUND INFECTION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMEMBRANOUS COLITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

SEPSIS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	   0 / 147 (0.00%)  0 / 0  0 / 0	   1 / 283 (0.35%)  0 / 1  0 / 1	
SEPTIC SHOCK alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	   1 / 147 (0.68%)  1 / 1  0 / 0	   0 / 283 (0.00%)  0 / 0  0 / 0	
UPPER RESPIRATORY TRACT INFECTION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	   0 / 147 (0.00%)  0 / 0  0 / 0	   1 / 283 (0.35%)  0 / 1  0 / 0	
URINARY TRACT INFECTION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	   0 / 147 (0.00%)  0 / 0  0 / 0	   2 / 283 (0.71%)  1 / 2  0 / 0	
WOUND INFECTION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	   0 / 147 (0.00%)  0 / 0  0 / 0	   1 / 283 (0.35%)  1 / 1  0 / 0	
Metabolism and nutrition disorders HYPERGLYCAEMIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	   1 / 147 (0.68%)  0 / 1  0 / 0	   1 / 283 (0.35%)  0 / 1  0 / 0	
HYPONATRAEMIA alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INSULIN-REQUIRING TYPE 2 DIABETES MELLITUS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm 2: LOM	Arm 1 : LOM+Bv	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 147 (94.56%)	278 / 283 (98.23%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
COLORECTAL ADENOCARCINOMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	
PERITUMOURAL OEDEMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	
SKIN PAPILLOMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
Vascular disorders			

AORTIC DILATATION		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
DEEP VEIN THROMBOSIS		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
EMBOLISM		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	11 / 283 (3.89%)
occurrences (all)	3	11
FLUSHING		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
HAEMATOMA		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	6 / 283 (2.12%)
occurrences (all)	3	6
HOT FLUSH		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	2 / 283 (0.71%)
occurrences (all)	2	2
HYPERTENSION		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	64 / 147 (43.54%)	166 / 283 (58.66%)
occurrences (all)	64	166
HYPOTENSION		
alternative dictionary used:		
MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	5 / 283 (1.77%)
occurrences (all)	0	5
PHLEBITIS		
alternative dictionary used:		
MedDRA 18.1		

subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)	
occurrences (all)	0	3	
THROMBOPHLEBITIS SUPERFICIAL			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
VASCULITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
CHILLS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	3 / 283 (1.06%)	
occurrences (all)	2	3	
FACE OEDEMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	1 / 283 (0.35%)	
occurrences (all)	2	1	
FACIAL PAIN			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences (all)	0	2	
FATIGUE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	75 / 147 (51.02%)	198 / 283 (69.96%)	
occurrences (all)	75	198	
GAIT DISTURBANCE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	17 / 147 (11.56%)	24 / 283 (8.48%)	
occurrences (all)	17	24	
GENERAL PHYSICAL HEALTH DETERIORATION			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences (all)	1	1	
INFLUENZA LIKE ILLNESS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	8 / 283 (2.83%)	
occurrences (all)	2	8	
LOCALISED OEDEMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences (all)	0	2	
MALAISE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	6 / 147 (4.08%)	10 / 283 (3.53%)	
occurrences (all)	6	10	
NON-CARDIAC CHEST PAIN			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	4 / 283 (1.41%)	
occurrences (all)	0	4	
OEDEMA PERIPHERAL			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	19 / 147 (12.93%)	25 / 283 (8.83%)	
occurrences (all)	19	25	
PAIN			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
PYREXIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	6 / 147 (4.08%)	26 / 283 (9.19%)	
occurrences (all)	6	26	
Immune system disorders			
HYPERSENSITIVITY			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed occurrences (all)	1 / 147 (0.68%) 1	5 / 283 (1.77%) 5	
Social circumstances MENOPAUSE alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	1 / 147 (0.68%) 1	0 / 283 (0.00%) 0	
Reproductive system and breast disorders BENIGN PROSTATIC HYPERPLASIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
BREAST PAIN alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
DYSPAREUNIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
OVARIAN CYST alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
PELVIC PAIN alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
UTERINE HAEMORRHAGE alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	1 / 147 (0.68%) 1	1 / 283 (0.35%) 1	
VAGINAL DISCHARGE alternative dictionary used: MedDRA 18.1			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>VULVOVAGINAL PRURITUS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p> <p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p> <p>1 / 283 (0.35%)</p> <p>1</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>ASPIRATION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>COUGH</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>DYSPHONIA</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>DYSPNOEA</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>EPISTAXIS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>HICCUPS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>NASAL CONGESTION</p> <p>alternative dictionary used: MedDRA 18.1</p>	<p>1 / 147 (0.68%)</p> <p>1</p> <p>8 / 147 (5.44%)</p> <p>8</p> <p>2 / 147 (1.36%)</p> <p>2</p> <p>9 / 147 (6.12%)</p> <p>9</p> <p>2 / 147 (1.36%)</p> <p>2</p> <p>0 / 147 (0.00%)</p> <p>0</p>	<p>4 / 283 (1.41%)</p> <p>4</p> <p>18 / 283 (6.36%)</p> <p>18</p> <p>15 / 283 (5.30%)</p> <p>15</p> <p>30 / 283 (10.60%)</p> <p>30</p> <p>40 / 283 (14.13%)</p> <p>40</p> <p>2 / 283 (0.71%)</p> <p>2</p>	

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
NASAL DRYNESS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
OROPHARYNGEAL PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	11 / 283 (3.89%)
occurrences (all)	1	11
PNEUMONIA ASPIRATION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
PNEUMONITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	2 / 283 (0.71%)
occurrences (all)	4	2
PRODUCTIVE COUGH		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	3 / 283 (1.06%)
occurrences (all)	1	3
PULMONARY EMBOLISM		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	14 / 283 (4.95%)
occurrences (all)	3	14
PULMONARY FIBROSIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
RHINITIS ALLERGIC		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	4 / 283 (1.41%)
occurrences (all)	4	4

Psychiatric disorders			
AGITATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	5 / 283 (1.77%)	
occurrences (all)	1	5	
ANXIETY			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	7 / 147 (4.76%)	11 / 283 (3.89%)	
occurrences (all)	7	11	
BRADYPHRENIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
CONFUSIONAL STATE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	7 / 147 (4.76%)	12 / 283 (4.24%)	
occurrences (all)	7	12	
DELIRIUM			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 147 (1.36%)	3 / 283 (1.06%)	
occurrences (all)	2	3	
DELUSION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
DEPRESSION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	5 / 147 (3.40%)	13 / 283 (4.59%)	
occurrences (all)	5	13	
HALLUCINATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)	
occurrences (all)	0	3	
INSOMNIA			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	7 / 147 (4.76%)	14 / 283 (4.95%)	
occurrences (all)	7	14	
MANIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
PERSONALITY CHANGE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	3 / 283 (1.06%)	
occurrences (all)	1	3	
PSYCHOTIC DISORDER			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	
TERMINAL INSOMNIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	
Investigations			
BLOOD CHOLESTEROL INCREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	
BLOOD CREATINE PHOSPHOKINASE INCREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
CARBON MONOXIDE DIFFUSING CAPACITY DECREASED			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences (all)	1	1	
C-REACTIVE PROTEIN INCREASED			
alternative dictionary used: MedDRA 18.1			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>GAMMA-GLUTAMYLTRANSFERASE INCREASED</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>WEIGHT DECREASED</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>WEIGHT INCREASED</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p> <p>2 / 147 (1.36%)</p> <p>2</p> <p>5 / 147 (3.40%)</p> <p>5</p> <p>11 / 147 (7.48%)</p> <p>11</p>	<p>1 / 283 (0.35%)</p> <p>1</p> <p>3 / 283 (1.06%)</p> <p>3</p> <p>41 / 283 (14.49%)</p> <p>41</p> <p>32 / 283 (11.31%)</p> <p>32</p>	
<p>Injury, poisoning and procedural complications</p> <p>BRAIN CONTUSION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>CONTUSION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>FALL</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>INFUSION RELATED REACTION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>PNEUMOCEPHALUS</p> <p>alternative dictionary used: MedDRA 18.1</p>	<p>1 / 147 (0.68%)</p> <p>1</p> <p>1 / 147 (0.68%)</p> <p>1</p> <p>2 / 147 (1.36%)</p> <p>2</p> <p>0 / 147 (0.00%)</p> <p>0</p>	<p>0 / 283 (0.00%)</p> <p>0</p> <p>2 / 283 (0.71%)</p> <p>2</p> <p>14 / 283 (4.95%)</p> <p>14</p> <p>1 / 283 (0.35%)</p> <p>1</p>	

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
RIB FRACTURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	
SPINAL FRACTURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	4 / 283 (1.41%)	
occurrences (all)	0	4	
SUBCUTANEOUS HAEMATOMA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
WOUND COMPLICATION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	7 / 283 (2.47%)	
occurrences (all)	1	7	
WOUND DEHISCENCE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	3 / 283 (1.06%)	
occurrences (all)	1	3	
WRIST FRACTURE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
Cardiac disorders			
ARRHYTHMIA SUPRAVENTRICULAR			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
CARDIAC FAILURE CONGESTIVE			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences (all)	1	1	
LEFT VENTRICULAR DYSFUNCTION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
MYOCARDIAL INFARCTION			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)	
occurrences (all)	0	2	
PALPITATIONS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences (all)	1	1	
SINUS BRADYCARDIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	2 / 283 (0.71%)	
occurrences (all)	1	2	
SINUS TACHYCARDIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 147 (2.04%)	1 / 283 (0.35%)	
occurrences (all)	3	1	
SUPRAVENTRICULAR TACHYCARDIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
VENTRICULAR ARRHYTHMIA			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
Nervous system disorders			
AMNESIA			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	3 / 147 (2.04%)	8 / 283 (2.83%)
occurrences (all)	3	8
APHASIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	24 / 147 (16.33%)	25 / 283 (8.83%)
occurrences (all)	24	25
APHONIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
APRAXIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
ATAXIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	11 / 283 (3.89%)
occurrences (all)	4	11
BRACHIAL PLEXOPATHY		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
BRAIN OEDEMA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	4 / 283 (1.41%)
occurrences (all)	0	4
CEREBRAL ISCHAEMIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
CEREBROSPINAL FLUID LEAKAGE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1

COGNITIVE DISORDER alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	10 / 147 (6.80%) 10	24 / 283 (8.48%) 24
DEPRESSED LEVEL OF CONSCIOUSNESS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	2 / 147 (1.36%) 2	6 / 283 (2.12%) 6
DISTURBANCE IN ATTENTION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	4 / 147 (2.72%) 4	13 / 283 (4.59%) 13
DIZZINESS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	19 / 147 (12.93%) 19	31 / 283 (10.95%) 31
DYSAESTHESIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	3 / 147 (2.04%) 3	1 / 283 (0.35%) 1
DYSARTHRIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	13 / 147 (8.84%) 13	11 / 283 (3.89%) 11
DYSGEUSIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	1 / 147 (0.68%) 1	7 / 283 (2.47%) 7
DYSKINESIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	3 / 283 (1.06%) 3
DYSLEXIA alternative dictionary used: MedDRA 18.1		

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
FACIAL NERVE DISORDER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	1 / 283 (0.35%)
occurrences (all)	2	1
FACIAL NEURALGIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
FACIAL PARESIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	5 / 147 (3.40%)	2 / 283 (0.71%)
occurrences (all)	5	2
HAEMORRHAGE INTRACRANIAL		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	6 / 283 (2.12%)
occurrences (all)	1	6
HEADACHE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	42 / 147 (28.57%)	98 / 283 (34.63%)
occurrences (all)	42	98
HEMIPARESIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	16 / 147 (10.88%)	27 / 283 (9.54%)
occurrences (all)	16	27
HYPERMOMNIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
HYPOAESTHESIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1

LETHARGY		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	4 / 283 (1.41%)
occurrences (all)	1	4
MEMORY IMPAIRMENT		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	15 / 147 (10.20%)	22 / 283 (7.77%)
occurrences (all)	15	22
MOTOR DYSFUNCTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
MUSCLE SPASTICITY		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	1 / 283 (0.35%)
occurrences (all)	2	1
NERVOUS SYSTEM DISORDER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
NEURALGIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
NEUROLOGIC NEGLECT SYNDROME		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
NEUROLOGICAL DECOMPENSATION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
OLFACTORY NERVE DISORDER		
alternative dictionary used: MedDRA 18.1		

subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
PARAESTHESIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	7 / 147 (4.76%)	10 / 283 (3.53%)
occurrences (all)	7	10
PAROSMIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
PERIPHERAL MOTOR NEUROPATHY		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	7 / 147 (4.76%)	16 / 283 (5.65%)
occurrences (all)	7	16
PERIPHERAL SENSORY NEUROPATHY		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	31 / 283 (10.95%)
occurrences (all)	2	31
PYRAMIDAL TRACT SYNDROME		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
QUADRANOPIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	2 / 283 (0.71%)
occurrences (all)	2	2
SEIZURE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	28 / 147 (19.05%)	70 / 283 (24.73%)
occurrences (all)	28	70
SOMNOLENCE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	6 / 147 (4.08%)	7 / 283 (2.47%)
occurrences (all)	6	7

<p>SYNCOPE</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>3 / 283 (1.06%)</p> <p>3</p>	
<p>TRANSIENT ISCHAEMIC ATTACK</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>TREMOR</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 147 (2.72%)</p> <p>4</p>	<p>6 / 283 (2.12%)</p> <p>6</p>	
<p>VIIIITH NERVE LESION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>Blood and lymphatic system disorders</p> <p>FEBRILE NEUTROPENIA</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>THROMBOTIC THROMBOCYTOPENIC PURPURA</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>0 / 283 (0.00%)</p> <p>0</p>	
<p>Ear and labyrinth disorders</p> <p>EAR PAIN</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>4 / 283 (1.41%)</p> <p>4</p>	
<p>EXTERNAL EAR INFLAMMATION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>HEARING IMPAIRED</p>			

<p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>8 / 283 (2.83%)</p> <p>8</p>	
<p>TINNITUS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 147 (2.72%)</p> <p>4</p>	<p>2 / 283 (0.71%)</p> <p>2</p>	
<p>VERTIGO</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>3 / 283 (1.06%)</p> <p>3</p>	
<p>Eye disorders</p> <p>BLINDNESS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>2 / 283 (0.71%)</p> <p>2</p>	
<p>BLINDNESS UNILATERAL</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>DIPLOPIA</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 147 (1.36%)</p> <p>2</p>	<p>0 / 283 (0.00%)</p> <p>0</p>	
<p>DRY EYE</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 147 (1.36%)</p> <p>2</p>	<p>2 / 283 (0.71%)</p> <p>2</p>	
<p>EXTRAOCULAR MUSCLE PARESIS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 147 (1.36%)</p> <p>2</p>	<p>2 / 283 (0.71%)</p> <p>2</p>	
<p>EYE PAIN</p> <p>alternative dictionary used: MedDRA 18.1</p>			

subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
EYELID DISORDER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
GLAUCOMA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
LACRIMATION INCREASED		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)
occurrences (all)	0	3
NIGHT BLINDNESS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
OPTIC NERVE DISORDER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	12 / 147 (8.16%)	20 / 283 (7.07%)
occurrences (all)	12	20
PERIORBITAL OEDEMA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
PHOTOPHOBIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	2 / 283 (0.71%)
occurrences (all)	2	2
PHOTOPSIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1

<p>RETINOPATHY</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>VISION BLURRED</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>7 / 147 (4.76%)</p> <p>7</p>	<p>12 / 283 (4.24%)</p> <p>12</p>	
<p>VISUAL ACUITY REDUCED</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>VISUAL IMPAIRMENT</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>Gastrointestinal disorders</p> <p>ABDOMINAL DISTENSION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>0 / 283 (0.00%)</p> <p>0</p>	
<p>ABDOMINAL PAIN</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 147 (1.36%)</p> <p>2</p>	<p>18 / 283 (6.36%)</p> <p>18</p>	
<p>ABDOMINAL PAIN UPPER</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>8 / 283 (2.83%)</p> <p>8</p>	
<p>ANAL FISSURE</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>ANAL FISTULA</p> <p>alternative dictionary used: MedDRA 18.1</p>			

subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
COLITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
CONSTIPATION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	20 / 147 (13.61%)	54 / 283 (19.08%)
occurrences (all)	20	54
DIARRHOEA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	10 / 147 (6.80%)	45 / 283 (15.90%)
occurrences (all)	10	45
DRY MOUTH		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	6 / 283 (2.12%)
occurrences (all)	2	6
DUODENAL ULCER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
DYSPEPSIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	6 / 283 (2.12%)
occurrences (all)	2	6
DYSPHAGIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	11 / 283 (3.89%)
occurrences (all)	2	11
ENTEROCOLITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2

FAECAL INCONTINENCE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	4 / 283 (1.41%)
occurrences (all)	0	4
GASTRITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	3 / 283 (1.06%)
occurrences (all)	1	3
GASTROINTESTINAL INFLAMMATION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
GASTROINTESTINAL PERFORATION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
GASTROOESOPHAGEAL REFLUX DISEASE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	9 / 283 (3.18%)
occurrences (all)	4	9
GINGIVAL PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	2 / 283 (0.71%)
occurrences (all)	1	2
HAEMORRHOIDAL HAEMORRHAGE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
HAEMORRHOIDS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	7 / 283 (2.47%)
occurrences (all)	3	7
HIATUS HERNIA		
alternative dictionary used: MedDRA 18.1		

subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
HYPOAESTHESIA ORAL		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
INGUINAL HERNIA STRANGULATED		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
LARGE INTESTINE PERFORATION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)
occurrences (all)	0	3
MOUTH HAEMORRHAGE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	5 / 283 (1.77%)
occurrences (all)	0	5
NAUSEA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	25 / 147 (17.01%)	70 / 283 (24.73%)
occurrences (all)	25	70
OESOPHAGEAL PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	9 / 283 (3.18%)
occurrences (all)	1	9
OESOPHAGITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
ORAL DYSAESTHESIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1

ORAL PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
PERIODONTAL DISEASE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	9 / 283 (3.18%)
occurrences (all)	0	9
RECTAL HAEMORRHAGE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	4 / 283 (1.41%)
occurrences (all)	1	4
SALIVARY HYPERSECRETION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
STOMATITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	5 / 147 (3.40%)	30 / 283 (10.60%)
occurrences (all)	5	30
TOOTH DEVELOPMENT DISORDER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
TOOTH LOSS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
TOOTHACHE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	16 / 283 (5.65%)
occurrences (all)	0	16
VOMITING		
alternative dictionary used: MedDRA 18.1		

subjects affected / exposed occurrences (all)	12 / 147 (8.16%) 12	33 / 283 (11.66%) 33	
Hepatobiliary disorders BILE DUCT STENOSIS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)  PORTAL HYPERTENSION alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	 1 / 147 (0.68%) 1  0 / 147 (0.00%) 0	 0 / 283 (0.00%) 0  1 / 283 (0.35%) 1	
Skin and subcutaneous tissue disorders ALOPECIA alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)  DECUBITUS ULCER alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)  DERMATITIS ACNEIFORM alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)  DERMATITIS BULLOUS alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)  DRY SKIN alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)  ERYTHEMA alternative dictionary used: MedDRA 18.1	 1 / 147 (0.68%) 1  0 / 147 (0.00%) 0  2 / 147 (1.36%) 2  1 / 147 (0.68%) 1  0 / 147 (0.00%) 0	 11 / 283 (3.89%) 11  1 / 283 (0.35%) 1  4 / 283 (1.41%) 4  0 / 283 (0.00%) 0  10 / 283 (3.53%) 10	

subjects affected / exposed	2 / 147 (1.36%)	0 / 283 (0.00%)
occurrences (all)	2	0
ERYTHEMA MULTIFORME		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
NAIL DISORDER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
NAIL RIDGING		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ONYCHOCLASIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ONYCHOMADESIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
PAIN OF SKIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
PETECHIAE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	2 / 283 (0.71%)
occurrences (all)	1	2

<b>PRURITUS</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	5 / 147 (3.40%) 5	17 / 283 (6.01%) 17	
<b>PURPURA</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
<b>RASH</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	1 / 147 (0.68%) 1	0 / 283 (0.00%) 0	
<b>RASH MACULO-PAPULAR</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	3 / 147 (2.04%) 3	14 / 283 (4.95%) 14	
<b>SCAR PAIN</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	1 / 147 (0.68%) 1	1 / 283 (0.35%) 1	
<b>SKIN ATROPHY</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	1 / 283 (0.35%) 1	
<b>Renal and urinary disorders</b> <b>ACUTE KIDNEY INJURY</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 147 (0.00%) 0	2 / 283 (0.71%) 2	
<b>CYSTITIS NONINFECTIVE</b> alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	3 / 147 (2.04%) 3	8 / 283 (2.83%) 8	
<b>HAEMATURIA</b> alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	1 / 147 (0.68%)	4 / 283 (1.41%)
occurrences (all)	1	4
NEPHROLITHIASIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
POLLAKIURIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)
occurrences (all)	0	3
PROTEINURIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
RENAL MASS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
URINARY INCONTINENCE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	12 / 283 (4.24%)
occurrences (all)	4	12
URINARY RETENTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	3 / 283 (1.06%)
occurrences (all)	1	3
URINARY TRACT OBSTRUCTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
URINARY TRACT PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	3 / 283 (1.06%)
occurrences (all)	4	3

<p>Endocrine disorders</p> <p><b>CUSHINGOID</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 147 (2.04%)</p> <p>3</p>	<p>3 / 283 (1.06%)</p> <p>3</p>	
<p><b>GLUCOCORTICOID DEFICIENCY</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p><b>HYPERTHYROIDISM</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>0 / 283 (0.00%)</p> <p>0</p>	
<p><b>HYPOTHYROIDISM</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p><b>STEROID WITHDRAWAL SYNDROME</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p><b>ARTHRALGIA</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>9 / 147 (6.12%)</p> <p>9</p>	<p>34 / 283 (12.01%)</p> <p>34</p>	
<p><b>ARTHRITIS</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p><b>BACK PAIN</b></p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 147 (2.72%)</p> <p>4</p>	<p>18 / 283 (6.36%)</p> <p>18</p>	
<p><b>BONE PAIN</b></p>			

alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	6 / 283 (2.12%)
occurrences (all)	1	6
FLANK PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
GROIN PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
INTERVERTEBRAL DISC PROTRUSION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
JOINT RANGE OF MOTION DECREASED		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	0 / 283 (0.00%)
occurrences (all)	2	0
MUSCLE SPASMS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)
occurrences (all)	0	3
MUSCULAR WEAKNESS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	13 / 147 (8.84%)	34 / 283 (12.01%)
occurrences (all)	13	34
MUSCULOSKELETAL CHEST PAIN		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
MYALGIA		
alternative dictionary used: MedDRA 18.1		

subjects affected / exposed	4 / 147 (2.72%)	28 / 283 (9.89%)	
occurrences (all)	4	28	
NECK PAIN			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 147 (2.04%)	7 / 283 (2.47%)	
occurrences (all)	3	7	
OSTEOARTHRITIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
OSTEOPOROSIS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)	
occurrences (all)	1	1	
PAIN IN EXTREMITY			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	6 / 147 (4.08%)	25 / 283 (8.83%)	
occurrences (all)	6	25	
PAIN IN JAW			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
SOFT TISSUE DISORDER			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
TRISMUS			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
Infections and infestations			
ABSCCESS SOFT TISSUE			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ANORECTAL INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
APPENDICITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ARTHRITIS INFECTIVE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
BRONCHITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	11 / 283 (3.89%)
occurrences (all)	2	11
CHOLANGITIS INFECTIVE		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
CLOSTRIDIUM DIFFICILE INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
CYSTITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	4 / 283 (1.41%)
occurrences (all)	2	4
DEVICE RELATED INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2

DIVERTICULITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ENDOCARDITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ENTEROCOLITIS INFECTIOUS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	2 / 283 (0.71%)
occurrences (all)	2	2
EPIDIDYMITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
ESCHERICHIA URINARY TRACT INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	2 / 283 (0.71%)
occurrences (all)	0	2
EYE INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
GASTROENTERITIS VIRAL		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
GASTROINTESTINAL INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
GINGIVITIS		
alternative dictionary used: MedDRA 18.1		

subjects affected / exposed	0 / 147 (0.00%)	6 / 283 (2.12%)
occurrences (all)	0	6
HERPES ZOSTER		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	8 / 283 (2.83%)
occurrences (all)	2	8
INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
LOWER RESPIRATORY TRACT INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
LUNG INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	10 / 283 (3.53%)
occurrences (all)	3	10
MUCOSAL INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
NAIL INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	3 / 283 (1.06%)
occurrences (all)	0	3
NASOPHARYNGITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
ORAL CANDIDIASIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0

ORAL INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
OTITIS EXTERNA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	2 / 147 (1.36%)	0 / 283 (0.00%)
occurrences (all)	2	0
OTITIS MEDIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
PARONYCHIA		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
PENILE INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
PERIPHERAL NERVE INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)
occurrences (all)	1	0
PERITONITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
PHARYNGITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
RHINITIS		
alternative dictionary used: MedDRA 18.1		

subjects affected / exposed	3 / 147 (2.04%)	14 / 283 (4.95%)
occurrences (all)	3	14
SEPSIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	2 / 283 (0.71%)
occurrences (all)	1	2
SINUSITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	4 / 283 (1.41%)
occurrences (all)	0	4
SKIN INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	4 / 147 (2.72%)	6 / 283 (2.12%)
occurrences (all)	4	6
SOFT TISSUE INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
TOOTH INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	1 / 147 (0.68%)	1 / 283 (0.35%)
occurrences (all)	1	1
TRACHEITIS		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)
occurrences (all)	0	1
UPPER RESPIRATORY TRACT INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	8 / 283 (2.83%)
occurrences (all)	3	8
URINARY TRACT INFECTION		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	3 / 147 (2.04%)	14 / 283 (4.95%)
occurrences (all)	3	14

<p>VAGINAL INFECTION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>VULVOVAGINAL MYCOTIC INFECTION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>1 / 283 (0.35%)</p> <p>1</p>	
<p>WOUND INFECTION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 147 (0.68%)</p> <p>1</p>	<p>4 / 283 (1.41%)</p> <p>4</p>	
<p>Metabolism and nutrition disorders</p> <p>DECREASED APPETITE</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>9 / 147 (6.12%)</p> <p>9</p>	<p>33 / 283 (11.66%)</p> <p>33</p>	
<p>DEHYDRATION</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 147 (2.04%)</p> <p>3</p>	<p>0 / 283 (0.00%)</p> <p>0</p>	
<p>DIABETES MELLITUS</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 147 (1.36%)</p> <p>2</p>	<p>0 / 283 (0.00%)</p> <p>0</p>	
<p>GLUCOSE TOLERANCE IMPAIRED</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 147 (0.00%)</p> <p>0</p>	<p>2 / 283 (0.71%)</p> <p>2</p>	
<p>HYPERGLYCAEMIA</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 147 (2.72%)</p> <p>4</p>	<p>3 / 283 (1.06%)</p> <p>3</p>	
<p>HYPERURICAEMIA</p> <p>alternative dictionary used:</p>			

MedDRA 18.1			
subjects affected / exposed	0 / 147 (0.00%)	1 / 283 (0.35%)	
occurrences (all)	0	1	
INCREASED APPETITE			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 147 (0.68%)	0 / 283 (0.00%)	
occurrences (all)	1	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported