Clinical trial results:
An open-label early access phase IIIb study of trifluridine / tipiracil (S 95005/TAS-102) in patients with a pretreated metastatic colorectal cancer (PRECONNECT study).

Summary

EudraCT number	2016-002311-18
Trial protocol	ES BE PT PL SI FR SK BG HR IT RO
Global end of trial date	30 November 2020

Results information

Result version number	v1 (current)
This version publication date	06 November 2021
First version publication date	06 November 2021

Trial information

Trial identification

Sponsor protocol code	CL3-95005-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03306394
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes, France, 92284
Public contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 1.55.72.43.66, clinicaltrials@servier.com
Scientific contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 1.55.72.43.66, clinicaltrials@servier.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2020
Global end of trial reached?	Yes
Global end of trial date	30 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to collect additional safety data during treatment with trifluridine / tipiracil in patients with a pretreated metastatic colorectal cancer (mCRC).

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 70
Country: Number of subjects enrolled	Brazil: 55
Country: Number of subjects enrolled	Panama: 17
Country: Number of subjects enrolled	Turkey: 100
Country: Number of subjects enrolled	Ukraine: 12
Country: Number of subjects enrolled	Belgium: 45
Country: Number of subjects enrolled	Bulgaria: 12
Country: Number of subjects enrolled	Croatia: 16
Country: Number of subjects enrolled	France: 292
Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Italy: 161
Country: Number of subjects enrolled	Poland: 54
Country: Number of subjects enrolled	Portugal: 24
Country: Number of subjects enrolled	Romania: 30
Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	Slovenia: 4
Worldwide total number of subjects	914
EEA total number of subjects	660

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)	525
From 65 to 84 years	387
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Investigators were oncologists.

Pre-assignment

Screening details:

Male or female patients aged ≥18 years old with metastatic colorectal cancer (mCRC) previously treated by at least 2 prior regimens of standard chemotherapies for mCRC and was refractory or intolerant to those chemotherapies.
Of note, 916 patients were enrolled in the study: 914 were treated and 2 not treated.

Period 1

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

Arms

Arm title	S95005

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S95005
Investigational medicinal product code	
Other name	Trifluridine-tipiracil
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

S95005 was administered orally twice a day (35 mg/m²/dose) within 1 hour after completion of morning and evening meals, 5 days on/2 days off, over 2 weeks, followed by a 14-day rest.

Number of subjects in period 1	S95005
Started	914
Completed	0
Not completed	914
Physician decision	14
Adverse event, non-fatal	55
Study termination by sponsor	20
Progressive disease	736
Commercial availability of the product	68
Lost to follow-up	3
Non-medical reason	18

Baseline characteristics

Reporting groups	
Reporting group title	S95005

Reporting group description: -

Reporting group values	S95005	Total	
Number of subjects	914	914	
Age categorical Units: Subjects			
Adults (18-64 years)	525	525	
From 65-84 years	387	387	
85 years and over	2	2	
Age continuous Units: years			
arithmetic mean	61.5		
standard deviation	± 10.6	-	
Gender categorical Units: Subjects			
Female	373	373	
Male	541	541	

End points

End points reporting groups

Reporting group title	S95005

Reporting group description: -

Primary: Adverse events

End point title	Adverse events[1]

End point description:

The primary objective of this study was to collect additional safety data during treatment with trifluridine/tipiracil in patients with a pretreated mCRC.
The number of subjects affected by adverse events is given in the present endpoints section. Description of serious and non-serious adverse events is provided in the adverse events section.

End point type	Primary

End point timeframe:

See the section adverse events.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	S95005			
Subject group type	Reporting group			
Number of subjects analysed	914			
Units: Number of patients affected				
number (not applicable)	884			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events that occurred or worsened or became serious between the first and the last IMP intake + 35 days (both included).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	S95005

Reporting group description: -

Serious adverse events	S95005		
Total subjects affected by serious adverse events			
subjects affected / exposed	335 / 914 (36.65%)		
number of deaths (all causes)	87		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	9 / 914 (0.98%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Intracranial tumour haemorrhage			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Malignant ascites			
subjects affected / exposed	2 / 914 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	124 / 914 (13.57%)		
occurrences causally related to treatment / all	3 / 124		
deaths causally related to treatment / all	2 / 54		
Malignant pleural effusion			

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to biliary tract				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to bladder				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metastases to central nervous system				
subjects affected / exposed	20 / 914 (2.19%)			
occurrences causally related to treatment / all	0 / 20			
deaths causally related to treatment / all	0 / 3			
Metastases to kidney				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to liver				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metastases to lung				
subjects affected / exposed	4 / 914 (0.44%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 3			
Metastases to muscle				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to peritoneum				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metastases to pleura				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Metastases to retroperitoneum				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to spine				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Tumour associated fever				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastasis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour compression				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hypertension				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	6 / 914 (0.66%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Jugular vein thrombosis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	5 / 914 (0.55%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	1 / 5			
Chest pain				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General physical health deterioration				
subjects affected / exposed	20 / 914 (2.19%)			
occurrences causally related to treatment / all	3 / 20			
deaths causally related to treatment / all	0 / 8			
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Oedema peripheral				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	8 / 914 (0.88%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				

Perineal induration			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	2 / 914 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bronchopleural fistula			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	4 / 914 (0.44%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Epistaxis			
subjects affected / exposed	2 / 914 (0.22%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Interstitial lung disease				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	8 / 914 (0.88%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 3			
Pulmonary embolism				
subjects affected / exposed	10 / 914 (1.09%)			
occurrences causally related to treatment / all	2 / 10			
deaths causally related to treatment / all	0 / 0			
Pulmonary infarction				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory distress				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Anxiety disorder				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				

subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Delirium tremens				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device occlusion				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Blood creatinine increased				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Anaemia postoperative				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bladder injury				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Fall				
subjects affected / exposed	5 / 914 (0.55%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Incision site haematoma				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract stoma complication				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vascular access malfunction				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				

subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Myocardial infarction				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Coma hepatic				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Apraxia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cauda equina syndrome				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Epilepsy				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Headache				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Febrile convulsion				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuralgia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial aneurysm				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuropathy peripheral				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vertigo CNS origin				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	34 / 914 (3.72%)			
occurrences causally related to treatment / all	28 / 37			
deaths causally related to treatment / all	0 / 0			
Blood loss anaemia				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Anaemia of malignant disease				
subjects affected / exposed	4 / 914 (0.44%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Bone marrow failure				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile bone marrow aplasia				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	9 / 914 (0.98%)			
occurrences causally related to treatment / all	10 / 10			
deaths causally related to treatment / all	0 / 0			
Microcytic anaemia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphopenia				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	20 / 914 (2.19%)			
occurrences causally related to treatment / all	25 / 25			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				

subjects affected / exposed	5 / 914 (0.55%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Blindness unilateral			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal artery thrombosis			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	12 / 914 (1.31%)		
occurrences causally related to treatment / all	2 / 13		
deaths causally related to treatment / all	0 / 1		
Abdominal pain upper			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal strangulated hernia			

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	11 / 914 (1.20%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 2			
Anal haemorrhage				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	11 / 914 (1.20%)			
occurrences causally related to treatment / all	11 / 12			
deaths causally related to treatment / all	1 / 1			
Dysphagia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Faecaloma				

subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastric stenosis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal obstruction				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal toxicity				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal haemorrhage				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Impaired gastric emptying				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	16 / 914 (1.75%)			
occurrences causally related to treatment / all	2 / 16			
deaths causally related to treatment / all	0 / 3			
Intestinal perforation				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Large intestinal stenosis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant gastrointestinal obstruction				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Mouth ulceration				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Obstruction gastric				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 0			
Oesophageal varices haemorrhage				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic failure				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritoneocutaneous fistula				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	6 / 914 (0.66%)			
occurrences causally related to treatment / all	2 / 6			
deaths causally related to treatment / all	0 / 1			
Varices oesophageal				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	14 / 914 (1.53%)			
occurrences causally related to treatment / all	8 / 16			
deaths causally related to treatment / all	1 / 2			
Hepatobiliary disorders				
Bile duct obstruction				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bile duct stenosis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Biliary dilatation				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cholecystitis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholestasis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	10 / 914 (1.09%)			
occurrences causally related to treatment / all	2 / 10			
deaths causally related to treatment / all	1 / 4			
Mixed liver injury				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	10 / 914 (1.09%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 3			
Portal hypertension				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Chronic kidney disease				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	4 / 914 (0.44%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 1			
Calculus urinary				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Nephropathy toxic				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Proteinuria				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthritis reactive				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal sepsis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Abdominal wall abscess				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspergilloma				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial pyelonephritis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Biliary tract infection				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Biliary sepsis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis gangrenous				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis escherichia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus colitis				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endophthalmitis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia pyelonephritis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	4 / 914 (0.44%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Listeria sepsis				

subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver abscess			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lymphangitis			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Medical device site infection			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Muscle abscess			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic abscess			
subjects affected / exposed	4 / 914 (0.44%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Pneumonia			

subjects affected / exposed	21 / 914 (2.30%)			
occurrences causally related to treatment / all	4 / 21			
deaths causally related to treatment / all	0 / 3			
Pneumonia pseudomonal				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psoas abscess				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	2 / 914 (0.22%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyopneumothorax				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	5 / 914 (0.55%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 1			
Septic shock				
subjects affected / exposed	4 / 914 (0.44%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
Spinal cord infection				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Stenotrophomonas sepsis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis bacterial				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection staphylococcal				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	3 / 914 (0.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Cachexia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Decreased appetite				
subjects affected / exposed	5 / 914 (0.55%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	8 / 914 (0.88%)			
occurrences causally related to treatment / all	4 / 8			
deaths causally related to treatment / all	0 / 1			
Hypocalcaemia				
subjects affected / exposed	1 / 914 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoalbuminaemia				

subjects affected / exposed	2 / 914 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	3 / 914 (0.33%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Steroid diabetes			
subjects affected / exposed	1 / 914 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	S95005		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	839 / 914 (91.79%)		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	57 / 914 (6.24%)		
occurrences (all)	60		
Gamma-glutamyltransferase increased			
subjects affected / exposed	46 / 914 (5.03%)		
occurrences (all)	47		
Neutrophil count decreased			
subjects affected / exposed	58 / 914 (6.35%)		
occurrences (all)	96		
Weight decreased			
subjects affected / exposed	50 / 914 (5.47%)		
occurrences (all)	51		

Neoplasms benign, malignant and unspecified (incl cysts and polyps) Malignant neoplasm progression subjects affected / exposed occurrences (all)	 57 / 914 (6.24%) 58		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 234 / 914 (25.60%) 259 427 / 914 (46.72%) 845 65 / 914 (7.11%) 76		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	 171 / 914 (18.71%) 215 73 / 914 (7.99%) 84 165 / 914 (18.05%) 189		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea	 74 / 914 (8.10%) 87 92 / 914 (10.07%) 98 218 / 914 (23.85%) 290 		

subjects affected / exposed	268 / 914 (29.32%)		
occurrences (all)	367		
Vomiting			
subjects affected / exposed	152 / 914 (16.63%)		
occurrences (all)	202		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	145 / 914 (15.86%)		
occurrences (all)	157		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported