



Clinical trial results:

Sorafenib plus capecitabine activity assesment in patients with advanced pre-treated colorectal cancer

Summary

EudraCT number	2010-023695-91
Trial protocol	BE
Global end of trial date	20 December 2016

Results information

Result version number	v1 (current)
This version publication date	22 August 2021
First version publication date	22 August 2021
Summary attachment (see zip file)	Synopsis v2.0 (So More 2.0 synopsis EN.pdf)

Trial information

Trial identification

Sponsor protocol code	So More
-----------------------	---------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01290926
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut Jules Bordet
Sponsor organisation address	rue Héger Bordet 1, Bruxelles, Belgium, 1000
Public contact	Dr. Alain Hendlisz, Institut Jules Bordet, 32 025413196, alain.hendlisz@bordet.be
Scientific contact	Dr. Alain Hendlisz, Institut Jules Bordet, 32 025413196, alain.hendlisz@bordet.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2013
Global end of trial reached?	Yes
Global end of trial date	20 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- a) To obtain a preliminary assessment about the activity of the combination by estimating overall survival of the study population at a fixed time point (6 months)
- b) To compare as an exploratory analysis the overall survival of metabolic responders versus non-responders.

Protection of trial subjects:

Some of the eligibility criteria that the subjects had to meet to be entered in the trial were chosen in order to minimize the risk of severe adverse events. In addition, the protocol planned rules for treatment modifications in case of the occurrence of specific adverse events. All subjects were free to withdraw from the clinical trial at any time for any reason given and the study was conducted in agreement with the declaration of Helsinki. It was controlled that the patients received before inclusion in the trial all standard medications that could be of benefit for them.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 February 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	Belgium: 97
Worldwide total number of subjects	97
EEA total number of subjects	97

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)	63
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants must meet all the inclusion criteria and exhibit all the exclusion criteria on screening examination to be eligible to participate in the study.

Pre-assignment

Screening details:

Subjects with confirmed colorectal cancer that is metastatic or unresectable and for which standard curative or palliative measures do not exist or are no longer effective.

Period 1

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

Arms

Arm title	Investigational medicinal products
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	sorafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg in the morning, 400 mg in the evening
escalation to 400 mg twice daily
continuous; dosing 21 days (3 weeks)

Investigational medicinal product name	capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

850 mg/m² twice daily;
days 1-14; weeks 1-2

Number of subjects in period 1	Investigational medicinal products
Started	97
Completed	73
Not completed	24
Consent withdrawn by subject	5
Physician decision	3
No treatment (in eligible patients)	4
Adverse event, non-fatal	5

Progression before treatment	1
Concurrent illness preventing protocol treatment	3
Protocol deviation	3

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description:	
97 patients included	
92 patients included in final analysis (5 excluded from overall analysis)	
88 patients included in safety analysis (4 excluded from safety analysis and metabolic analysis)	
79 patients included in metabolic analysis (9 further excluded from metabolic analysis)	

Reporting group values	Overall trial	Total	
Number of subjects	97	97	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	63	63	
From 65-84 years	34	34	
85 years and over	0	0	
Age continuous			
Units: years			
median	63		
full range (min-max)	28 to 83	-	
Gender categorical			
Units: Subjects			
Female	43	43	
Male	54	54	

End points

End points reporting groups

Reporting group title	Investigational medicinal products
Reporting group description: -	
Subject analysis set title	Metabolic Response
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients were classified according to the lesional distribution of mR; Class 1: no metabolic unresponsive lesion; Class 2: minority of unresponsive lesion among whole body target tumour load; Class 3: majority of whole body target tumour load does not respond; Class 4: all target lesions are non-responding, or, presence of progressive lesions [progression defined as >25% increase of FDG uptake on second PET, or appearance of a new lesion]. MR data were available for 79 patients: 37 (46.8%) were classified as class I; 14 (17.7%) as class II; 11 (13.9%) as class III; and 17 (21.5%) as class IV. Within Class IV, 8 patients (10%) showed early metabolic disease progression.	
Subject analysis set title	Survival data
Subject analysis set type	Intention-to-treat
Subject analysis set description: This subject analysis set is used to assess OS and PFS. Patients were followed until objective disease progression and every 3 months thereafter for survival assessment.	
Subject analysis set title	Metabolic Response Class I
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with absence of any metabolically non-responding lesion	
Subject analysis set title	Metabolic Response Class II-III-IV
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with heterogeneous responses (minor part of whole body tumour load shows a non-response or major part of whole body target tumour load does not respond) and patients with all target lesions are non-responding, or presence of a progressive lesion.	
Primary: Overall Survival	
End point title	Overall Survival
End point description: Overall survival is defined as the time from start of therapy until death	
End point type	Primary
End point timeframe: start of therapy until death	

End point values	Metabolic Response	Survival data	Metabolic Response Class I	Metabolic Response Class II-III-IV
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	92	37 ^[1]	42 ^[2]
Units: months				
median (confidence interval 95%)	8.2 (6.8 to 10.5)	8.2 (6.8 to 10.5)	9.9 (7.6 to 16.3)	6.6 (4.9 to 8.3)

Notes:

[1] - MR Class I

[2] - MR class II-III-IV

Attachments (see zip file)	SoMore-multivariate.png
-----------------------------------	-------------------------

Statistical analyses

Statistical analysis title	Univariate and Multivariate analysis for OS/PFS
-----------------------------------	---

Statistical analysis description:

The multivariate analysis was performed using Cox's proportional hazard model. Variables with a univariate P-value < 0.20 were considered as possible predictors in the multivariate model. We performed stepwise forward selection of variables, i.e. forward selection but at each step variables already in the model could be dropped if their associated p-value became >0.05. To verify the final model, also backward selection of variables was performed on all variables with univariate p-value<0.20

Comparison groups	Metabolic Response Class I v Metabolic Response Class II-III-IV
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≥ 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Confidence interval	
level	95 %
sides	2-sided

Secondary: Progression free survival

End point title	Progression free survival
-----------------	---------------------------

End point description:

Progression free survival is defined as the interval between the start of treatment and the earliest date of disease progression or death due to any cause. Assessments of progression were made by investigator.

End point type	Secondary
----------------	-----------

End point timeframe:

start of therapy until disease progression

End point values	Metabolic Response	Survival data	Metabolic Response Class I	Metabolic Response Class II-III-IV
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	92	37	42
Units: months				
median (confidence interval 95%)	4.2 (3.4 to 4.8)	4.2 (3.4 to 4.8)	5 (4 to 8.9)	2.3 (1.3 to 3.1)

Attachments (see zip file)	SoMore-multivariate.png
-----------------------------------	-------------------------

Statistical analyses

Statistical analysis title	Univariate and Multivariate analysis for OS/PFS
-----------------------------------	---

Statistical analysis description:

The multivariate analysis was performed using Cox's proportional hazard model. Variables with a univariate P-value < 0.20 were considered as possible predictors in the multivariate model. We performed stepwise forward selection of variables, i.e. forward selection but at each step variables already in the model could be dropped if their associated p-value became >0.05. To verify the final model, also backward selection of variables was performed on all variables with univariate p-value<0.20

Comparison groups	Metabolic Response Class II-III-IV v Metabolic Response Class I
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≥ 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Confidence interval	
level	95 %
sides	2-sided

Secondary: Metabolic Response

End point title	Metabolic Response
-----------------	--------------------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

6 months after registration

End point values	Metabolic Response			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Number of patients				
Class I	37			
Class II	14			
Class III	11			
Class IV	17			

Attachments (see zip file)	somore.PNG
-----------------------------------	------------

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response

End point title	Overall response
-----------------	------------------

End point description:

Overall response is the number of participants who had a best outcome of a complete response (CR, all detectable tumour disappeared) or a partial response (PR, a $\geq 30\%$ decrease in the sum of the longest dimensions of the target lesions taking as a reference the baseline sum) per response evaluation criteria in solid tumours (RECIST v1.1) at some point during the study. Progressive disease (PD), a $\geq 20\%$ increase in target lesions.

RECIST radiological response was assessed locally every two cycles (6 weeks). Patients were followed until objective disease progression and every 3 months thereafter for survival assessment.

End point type	Secondary
----------------	-----------

End point timeframe:

baseline until either response or progression

End point values	Metabolic Response			
Subject group type	Subject analysis set			
Number of subjects analysed	77			
Units: Number of subjects				
Partial Response	4			
Stable Disease	52			
Progressive Disease	21			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the first administration of study treatments until 30 days after the last dose of study treatments.

Adverse event reporting additional description:

88 subjects were exposed to the investigational medicinal products.

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

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	19.1
--------------------	------

Reporting groups

Reporting group title	All serious adverse events
-----------------------	----------------------------

Reporting group description: -

Serious adverse events	All serious adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 88 (27.27%)		
number of deaths (all causes)	88		
number of deaths resulting from adverse events	3		
Investigations			
Weight decreased			
subjects affected / exposed	1 / 88 (1.14%)		
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	2 / 88 (2.27%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			

subjects affected / exposed	5 / 88 (5.68%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric perforation			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		
Large intestinal obstruction			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			

subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Gallbladder obstruction			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelocaliectasis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal failure			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Fistula			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Groin pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations Abdominal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 88 (1.14%) 0 / 1 0 / 0		
Abscess limb subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 88 (1.14%) 0 / 1 0 / 0		
Candida infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 88 (1.14%) 0 / 1 0 / 0		
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 88 (2.27%) 0 / 2 0 / 0		
Septic shock subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 88 (2.27%) 0 / 2 0 / 2		
Urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 88 (1.14%) 0 / 1 0 / 0		
Wound infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 88 (1.14%) 1 / 1 0 / 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 88 (2.27%) 0 / 2 0 / 0		

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

Non-serious adverse events	All serious adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 88 (98.86%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Tumour pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Embolism			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Haemorrhage			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	13 / 88 (14.77%)		
occurrences (all)	13		
Hypotension			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Thrombosis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Chest pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	71 / 88 (80.68%)		
occurrences (all)	93		
Hyperthermia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Mucosal inflammation			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	5		
Nodule			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	6 / 88 (6.82%)		
occurrences (all)	7		
Immune system disorders			
Hypersensitivity			

subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Pelvic pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Dysphonia			
subjects affected / exposed	10 / 88 (11.36%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	8 / 88 (9.09%)		
occurrences (all)	11		
Epistaxis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hiccups			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Rhinalgia			

subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Blood folate abnormal			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Blood phosphorus decreased			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	3		
Liver function test abnormal			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	5		
Protein total			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Weight decreased			

subjects affected / exposed occurrences (all)	23 / 88 (26.14%) 25		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Eschar			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Foot fracture			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Lower limb fracture			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Cardiac disorders			
Thrombocytopenia			
subjects affected / exposed	11 / 88 (12.50%)		
occurrences (all)	18		
Myocardial ischaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Balance disorder			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Headache			

subjects affected / exposed	6 / 88 (6.82%)		
occurrences (all)	9		
Hypoaesthesia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Peripheral motor neuropathy			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	11 / 88 (12.50%)		
occurrences (all)	13		
Sciatica			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	22 / 88 (25.00%)		
occurrences (all)	27		
Leukopenia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	7		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	2		
Periorbital oedema			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Abdominal pain			

subjects affected / exposed	14 / 88 (15.91%)		
occurrences (all)	18		
Abdominal pain lower			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Ascites			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Colitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	22 / 88 (25.00%)		
occurrences (all)	29		
Diarrhoea			
subjects affected / exposed	55 / 88 (62.50%)		
occurrences (all)	97		
Dry mouth			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Dysphagia			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Enterovesical fistula			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Gastrointestinal pain			

subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Intestinal obstruction			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	26 / 88 (29.55%)		
occurrences (all)	34		
Pancreatitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	29 / 88 (32.95%)		
occurrences (all)	35		
Vomiting			
subjects affected / exposed	16 / 88 (18.18%)		
occurrences (all)	25		
Genital herpes			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hepatic pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		

Hepatomegaly			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Hyperbilirubinaemia			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Jaundice			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 88 (9.09%)		
occurrences (all)	8		
Dry skin			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hair colour changes			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Nail disorder			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	58 / 88 (65.91%)		
occurrences (all)	79		
Pruritus			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	14 / 88 (15.91%)		
occurrences (all)	15		
Renal and urinary disorders			

Acute kidney injury subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Dysuria subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Haematuria subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Renal failure subjects affected / exposed occurrences (all)	2 / 88 (2.27%) 1		
Urinary retention subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Endocrine disorders Hyperparathyroidism subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 7		
Back pain subjects affected / exposed occurrences (all)	4 / 88 (4.55%) 5		
Bone pain subjects affected / exposed occurrences (all)	2 / 88 (2.27%) 2		
Foot deformity subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Limb discomfort subjects affected / exposed occurrences (all)	1 / 88 (1.14%) 1		
Muscle spasms			

subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	3		
Muscular weakness			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	3		
Infections and infestations			
Clostridium difficile infection			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		

Herpes virus infection			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Parotitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Rectal abscess			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	46 / 88 (52.27%)		
occurrences (all)	63		
Dehydration			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hyperuricaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hypocalcaemia			

subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2011	Increasing of the sample size => protocol v2.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

There were no limitations and caveats applicable to this summary of the results.
--

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/27072811>