Clinical trial results:
Phase III Double-blinded, Placebo Controlled Study of Xilonix for Improving Survival in Metastatic Colorectal Cancer

Summary

EudraCT number	2012-005287-10
Trial protocol	HU PL BE CZ ES AT DE NL GB IT
Global end of trial date	09 June 2017

Results information

Result version number	v1 (current)
This version publication date	09 April 2021
First version publication date	09 April 2021

Trial information

Trial identification

Sponsor protocol code	2012-PT023

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01767857
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, United States, NJ 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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	09 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 June 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the overall survival (OS) which was measured from the date of randomization until death or last follow-up.

Protection of trial subjects:

The study was performed in accordance with the current version of the declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013). The trial was conducted in compliance with the International Conference on Harmonization (ICH) guidelines on Good Clinical Practice (GCP). The safety data was monitored every 6 months or after every 200 subjects of accrual.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	Austria: 15
Country: Number of subjects enrolled	Belgium: 76
Country: Number of subjects enrolled	Czechia: 11
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 18
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Poland: 48
Country: Number of subjects enrolled	Spain: 173
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 199
Worldwide total number of subjects	611
EEA total number of subjects	364

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)	351
From 65 to 84 years	258
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

611 subjects were randomized (modified intent to treat population [mITT] population) and analyzed for efficacy and safety.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Xilonix

Arm description:

Subjects received 7.5 milligram per kilogram (mg/kg) Xilonix (MABp1) via intravenous (IV) injection once every 2 weeks until evidence of radiographic or clinical progression along with best supportive care (BSC) (up to 18 months).

Arm type	Experimental
Investigational medicinal product name	Xilonix
Investigational medicinal product code	
Other name	MABp1
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Xilonix was administered as IV injection of 7.5 mg/kg once every 2 weeks (one cycle) until evidence of radiographic or clinical progression.

Arm title	Placebo

Arm description:

Subjects received placebo via IV injection once every 2 weeks until evidence of radiographic or clinical progression plus BSC (up to 18 months).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was administered as IV injection until evidence of radiographic or clinical progression.

Number of subjects in period 1	Xilonix	Placebo
Started	411	200
Completed	0	0
Not completed	411	200
Adverse event, serious fatal	35	16
Physician decision	17	10
Consent withdrawn by subject	38	18
Adverse event, non-fatal	20	4
Protocol terminated	1	-
Lost to follow-up	1	1
Lack of efficacy	299	151

Baseline characteristics

Reporting groups	
Reporting group title	Xilonix
Reporting group description:	
Subjects received 7.5 milligram per kilogram (mg/kg) Xilonix (MABp1) via intravenous (IV) injection once every 2 weeks until evidence of radiographic or clinical progression along with best supportive care (BSC) (up to 18 months).	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo via IV injection once every 2 weeks until evidence of radiographic or clinical progression plus BSC (up to 18 months).	

Reporting group values	Xilonix	Placebo	Total
Number of subjects	411	200	611
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	229	122	351
From 65 to 84 years	181	77	258
85 years and over	1	1	2
Title for AgeContinuous			
Units: years			
arithmetic mean	62.9	61.1	
standard deviation	± 10.14	± 9.98	-
Title for Gender			
Units: subjects			
Female	159	94	253
Male	252	106	358

End points

End points reporting groups

Reporting group title	Xilonix
Reporting group description:	
Subjects received 7.5 milligram per kilogram (mg/kg) Xilonix (MABp1) via intravenous (IV) injection once every 2 weeks until evidence of radiographic or clinical progression along with best supportive care (BSC) (up to 18 months).	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo via IV injection once every 2 weeks until evidence of radiographic or clinical progression plus BSC (up to 18 months).	

Primary: Overall survival (OS)

End point title	Overall survival (OS)
End point description:	
Overall survival time was defined as the duration from the date of randomization until death or last follow-up. OS was summarized by Kaplan-Meier method and compared between the treatment groups using un-adjusted log-rank test. The modified intent-to-treat (mITT) population consisted of subjects who were randomized and received at least one infusion of study drug.	
End point type	Primary
End point timeframe:	
Up to 18 months	

End point values	Xilonix	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	200		
Units: Months				
median (confidence interval 95%)	5.6 (4.9 to 6.2)	5.4 (4.6 to 6.2)		

Statistical analyses

Statistical analysis title	Statistical Analaysis
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	611
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.613
Method	Logrank

Secondary: Change from Baseline in Lean Body Mass (LBM) Measured by Dual-energy X-ray Absorptiometry (DEXA) Scans

End point title	Change from Baseline in Lean Body Mass (LBM) Measured by Dual-energy X-ray Absorptiometry (DEXA) Scans

End point description:

Change from baseline in LBM as measured by Dexa scans was reported. DEXA is an X-ray imaging modality used to determine the mass of one material in the presence of another material, using the knowledge of their unique X-ray attenuation at different energies. The per protocol (PP) population was defined as subjects that had baseline and follow up values for both the DEXA assessment and the European Organization for Research and Treatment of Cancer (EORTC) questionnaire.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Xilonix	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	94		
Units: kilogram (Kg)				
least squares mean (standard error)	0.51 (± 0.158)	-0.21 (± 0.231)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANCOVA

Secondary: Change from Baseline in Symptom Scale and Global Health Status/Quality of Life (QoL) Assessed Through the Cancer-specific European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire (EORTC QLQ-C30)

End point title	Change from Baseline in Symptom Scale and Global Health Status/Quality of Life (QoL) Assessed Through the Cancer-specific European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire (EORTC QLQ-C30)

End point description:

The EORTC QLQ-C30 questionnaire incorporates nine multi-item scales: 5 functional scales (physical, cognitive, role, emotional, and social); 3 symptom scales (pain, fatigue, and appetite loss) and a Global Health Status/QoL scale. Each item, except Global Health Status, is answered on a four-point scale (0-4): 1-not at all, 2-a little, 3-quite a bit, 4-very much. Response to Global Health Status is measured on a 1 to 7 scale. "1" being very poor and "7" being excellent. As planned, the data for symptom scales (pain, fatigue, appetite loss) and a Global Health Status/QoL scale was evaluated and reported. The PP population was defined as subjects that had baseline and follow up values for both the DEXA assessment and the EORTC questionnaire.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Xilonix	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	94		
Units: Units on a scale				
least squares mean (standard error)				
Global Health Status/Qol	-6.64 (± 1.392)	-8.16 (± 2.041)		
Pain	8.50 (± 1.707)	10.27 (± 2.503)		
Fatigue	7.42 (± 1.516)	8.82 (± 2.223)		
Appetite Loss	9.34 (± 2.010)	11.84 (± 2.947)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Global Health Status/Qol
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.541
Method	ANCOVA

Statistical analysis title	Statistical Analysis for Pain
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56
Method	ANCOVA

Statistical analysis title	Statistical Analysis for Fatigue
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.603
Method	ANCOVA

Statistical analysis title	Statistical Analysis for Appetite Loss
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.485
Method	ANCOVA

Secondary: Change from Baseline in Platelet Counts

End point title	Change from Baseline in Platelet Counts

End point description:

Change from baseline in platelet counts up to Week 8 was evaluated. The PP population was defined as subjects that had baseline and follow up values for both the DEXA assessment and the EORTC questionnaire.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Xilonix	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	94		
Units: 1000 cells/cubic millimeter				
least squares mean (standard error)	5.50 (± 4.721)	16.19 (± 7.082)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Xilonix v Placebo
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	ANCOVA

Secondary: Percentage of Subjects with Objective Response (OR)

End point title	Percentage of Subjects with Objective Response (OR)

End point description:

The percentage of OR was estimated by dividing the total number of confirmed complete response (CR) and partial response (PR) by the total number of subjects randomized where CR was complete disappearance of all lesions (whether measurable or not, and no new lesions); confirmation by a repeat, consecutive assessment no less than 4 weeks from the date first documented and PR was decrease in

tumor burden greater than or equal to (>=) 50 percent (%) relative to baseline confirmed by a consecutive assessment at least 4 weeks after first documentation. The mITT population consisted of subjects who were randomized and received at least one infusion of study drug.

End point type	Secondary

End point timeframe:

Up to 18 months

End point values	Xilonix	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	200		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Disease Control

End point title	Percentage of Subjects with Disease Control

End point description:

Percentage of subjects who achieved disease control was estimated by dividing total number of confirmed CRs, PRs and stable disease (SD) by total number of subjects randomized. CR was complete disappearance of all lesions (whether measurable or not, and no new lesions); confirmed by repeat, consecutive assessment no less than (<) 4 weeks from date first documented, PR was decrease in tumor burden >= 50% relative to baseline confirmed by consecutive assessment at least 4 weeks after first documentation. SD defined as not meeting criteria for CR and PR, in absence of Progressive Disease (increase in tumor burden >= 25 % relative to nadir [minimum recorded tumor burden] confirmed by repeat, consecutive assessment no < 4 weeks from date first documented). The subjects with baseline and follow up radiographic assessments were included in this analysis.

End point type	Secondary

End point timeframe:

Up to 18 months

End point values	Xilonix	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	154		
Units: Percentage of Subjects				
number (not applicable)	25	27.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 18 months

Adverse event reporting additional description:

Safety analysis included the safety population, defined as enrolled subjects who received at least one dose of study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo via IV injection once every 2 weeks until evidence of radiographic or clinical progression plus best supportive care (BSC) (up to 18 months).

Reporting group title	Xilonix

Reporting group description:

Subjects received 7.5 milligram per kilogram (mg/kg) Xilonix (MABp1) via intravenous (IV) injection once every 2 weeks until evidence of radiographic or clinical progression along with best supportive care (BSC) (up to 18 months).

Serious adverse events	Placebo	Xilonix	
Total subjects affected by serious adverse events			
subjects affected / exposed	84 / 200 (42.00%)	169 / 411 (41.12%)	
number of deaths (all causes)	41	78	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bone Neoplasm			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer Pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon Cancer			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal Cancer			
subjects affected / exposed	5 / 200 (2.50%)	8 / 411 (1.95%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 2	0 / 4	
Colorectal Cancer Metastatic			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Neoplasm Progression			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Pleural Effusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to Central Nervous System			
subjects affected / exposed	4 / 200 (2.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm Progression			
subjects affected / exposed	2 / 200 (1.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic Neoplasm			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory Collapse			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep Vein Thrombosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Pain Management			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral Stent Removal			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse Drug Reaction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	2 / 200 (1.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chest Pain			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 200 (0.50%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	

Disease Progression			
subjects affected / exposed	14 / 200 (7.00%)	21 / 411 (5.11%)	
occurrences causally related to treatment / all	0 / 14	0 / 21	
deaths causally related to treatment / all	0 / 5	0 / 7	
Fatigue			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General Physical Health Deterioration			
subjects affected / exposed	5 / 200 (2.50%)	8 / 411 (1.95%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Localised Oedema			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema Peripheral			
subjects affected / exposed	0 / 200 (0.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 200 (0.00%)	5 / 411 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance Status Decreased			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	1 / 200 (0.50%)	6 / 411 (1.46%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Failure			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 200 (0.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	9 / 200 (4.50%)	12 / 411 (2.92%)	
occurrences causally related to treatment / all	0 / 10	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	2 / 200 (1.00%)	5 / 411 (1.22%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			

subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	2 / 200 (1.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 200 (0.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed Suicide			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional State			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Bilirubin Increased			
subjects affected / exposed	2 / 200 (1.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Culture Positive			

subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Stoma Complication			
subjects affected / exposed	2 / 200 (1.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion Related Reaction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	2 / 200 (1.00%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma Site Haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic Vertebral Fracture			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to Various Agents			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Stoma Complication			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urostomy Complication			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial Effusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance Disorder			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Oedema			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of Consciousness			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Cord Compression			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 200 (2.50%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	1 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	6 / 200 (3.00%)	9 / 411 (2.19%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal Stenosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 200 (0.00%)	7 / 411 (1.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 200 (0.50%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Haemorrhage			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Perforation			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 200 (1.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	2 / 200 (1.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestinal Obstruction			
subjects affected / exposed	0 / 200 (0.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Bowel Obstruction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	3 / 200 (1.50%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal Haemorrhage			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal Varices Haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Stenosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Haemorrhage			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	1 / 200 (0.50%)	6 / 411 (1.46%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Haemorrhage			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 200 (1.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile Duct Obstruction			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile Duct Stenosis			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Failure			
subjects affected / exposed	3 / 200 (1.50%)	11 / 411 (2.68%)	
occurrences causally related to treatment / all	0 / 3	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 200 (1.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice Cholestatic			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Disorder			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 200 (0.50%)	8 / 411 (1.95%)	
occurrences causally related to treatment / all	0 / 1	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 200 (0.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 200 (0.50%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure			

subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Incontinence			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Pain			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal Pain			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in Extremity			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Pain			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Abdominal Abscess			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter Site Abscess			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter Site Infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney Infection			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 200 (1.00%)	5 / 411 (1.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Staphylococcal			

subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	1 / 200 (0.50%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 200 (2.00%)	3 / 411 (0.73%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Infection			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis Septic			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 200 (0.50%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	0 / 200 (0.00%)	2 / 411 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Infection			

subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 411 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to Thrive			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 411 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Xilonix	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	167 / 200 (83.50%)	324 / 411 (78.83%)	
Investigations			
Aspartate Aminotransferase Increased			
subjects affected / exposed	6 / 200 (3.00%)	23 / 411 (5.60%)	
occurrences (all)	6	29	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	13 / 200 (6.50%)	20 / 411 (4.87%)	
occurrences (all)	14	24	
Blood Bilirubin Increased			
subjects affected / exposed	7 / 200 (3.50%)	25 / 411 (6.08%)	
occurrences (all)	9	31	
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 200 (7.50%)	25 / 411 (6.08%)	
occurrences (all)	16	34	
Cardiac disorders			
Sinus Tachycardia			
subjects affected / exposed	10 / 200 (5.00%)	11 / 411 (2.68%)	
occurrences (all)	13	14	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 200 (6.50%)	21 / 411 (5.11%)	
occurrences (all)	18	24	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	20 / 200 (10.00%)	42 / 411 (10.22%)	
occurrences (all)	26	62	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	35 / 200 (17.50%)	63 / 411 (15.33%)	
occurrences (all)	58	91	
Fatigue			
subjects affected / exposed	60 / 200 (30.00%)	109 / 411 (26.52%)	
occurrences (all)	75	139	
Oedema Peripheral			

subjects affected / exposed	23 / 200 (11.50%)	39 / 411 (9.49%)	
occurrences (all)	23	49	
Pyrexia			
subjects affected / exposed	27 / 200 (13.50%)	38 / 411 (9.25%)	
occurrences (all)	39	47	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	41 / 200 (20.50%)	78 / 411 (18.98%)	
occurrences (all)	55	95	
Constipation			
subjects affected / exposed	31 / 200 (15.50%)	51 / 411 (12.41%)	
occurrences (all)	34	63	
Diarrhoea			
subjects affected / exposed	22 / 200 (11.00%)	45 / 411 (10.95%)	
occurrences (all)	29	64	
Nausea			
subjects affected / exposed	46 / 200 (23.00%)	79 / 411 (19.22%)	
occurrences (all)	57	112	
Vomiting			
subjects affected / exposed	20 / 200 (10.00%)	46 / 411 (11.19%)	
occurrences (all)	24	61	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	27 / 200 (13.50%)	40 / 411 (9.73%)	
occurrences (all)	30	43	
Dyspnoea			
subjects affected / exposed	27 / 200 (13.50%)	49 / 411 (11.92%)	
occurrences (all)	39	60	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	10 / 200 (5.00%)	16 / 411 (3.89%)	
occurrences (all)	10	17	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	11 / 200 (5.50%)	11 / 411 (2.68%)	
occurrences (all)	15	11	

Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	27 / 200 (13.50%)	44 / 411 (10.71%)	
occurrences (all)	31	50	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	51 / 200 (25.50%)	84 / 411 (20.44%)	
occurrences (all)	58	99	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2014	This amendment was proposed to the FDA to enable faster patient recruitment by employing a more traditional Phase 3 oncology design.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 July 2014	The agency placed the program on a partial clinical hold to discuss changes to the protocol, as well as manufacturing changes.	15 September 2015

Notes:

Limitations and caveats

None reported