



Clinical trial results:

A Randomized, Double-Blind, Phase 3 Study of the JAK1/2 Inhibitor Ruxolitinib or Placebo in Combination With Capecitabine in Subjects With Advanced or Metastatic Adenocarcinoma of the Pancreas Who Have Failed or Are Intolerant to First-Line Chemotherapy (The JANUS 2 Study)

Summary

EudraCT number	2014-000294-39
Trial protocol	SE AT DK PT NL FR IE
Global end of trial date	14 October 2016

Results information

Result version number	v1 (current)
This version publication date	02 November 2017
First version publication date	02 November 2017

Trial information

Trial identification

Sponsor protocol code	INCB 18424-363
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02119663
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cut-Off, Wilmington, DE, United States, 19803
Public contact	Incyte Corporation Call Centre, Incyte Corporation, +44 (0)330 100 3677, globalmedinfo@incyte.com
Scientific contact	Incyte Corporation Call Centre, Incyte Corporation, +44 (0)330 100 3677, globalmedinfo@incyte.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	Interim
Date of interim/final analysis	13 April 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 October 2016
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 evaluate and compare the overall survival (OS) of subjects with advanced or metastatic adenocarcinoma of the pancreas when treated with ruxolitinib in combination with Capecitabine versus Capecitabine alone.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2014
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	Mexico: 2
Country: Number of subjects enrolled	Chile: 5
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	United States: 50
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Ireland: 1
Worldwide total number of subjects	86
EEA total number of subjects	19

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)	28
From 65 to 84 years	56
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 51 study centers (24 in the United States [US], 4 in Austria, 4 in Israel, 3 in the Netherlands, 3 in Portugal, 2 in Argentina, 2 in Chile, 2 in Denmark, 2 in France, 2 in Mexico, 2 in Switzerland, and 1 in Ireland).

Pre-assignment

Screening details:

Subjects with advanced or metastatic adenocarcinoma of the pancreas who had failed or were intolerant to first-line chemotherapy were screened for up to 28 days to determine eligibility before randomization to one of the treatment groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ruxolitinib plus Capecitabine

Arm description:

Ruxolitinib 15 mg in combination with a starting dose of Capecitabine 2000 mg/m² administered orally twice daily (BID).

Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	
Other name	Jakafi ®, Jakavi ®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ruxolitinib 5 mg tablets administered at a dose of 15 mg twice daily (BID).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capecitabine self-administered orally, BID, approximately 12 hours apart, for the first 14 days of each 21-day study cycle. Doses of Capecitabine administered as the appropriate number of 150 mg or 500 mg tablets.

Arm title	Placebo Plus Capecitabine
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Arm description:

Placebo tablets in combination with a starting dose of Capecitabine 2000 mg/m².

Arm type	Active comparator
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets to be administered by mouth twice daily (BID).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg or 500 mg tablets to be administered by mouth twice daily (BID).

Number of subjects in period 1	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine
Started	43	43
Completed	3	2
Not completed	40	41
Adverse event, serious fatal	3	2
Physician decision	1	2
Disease progression	26	27
Other unspecified	2	-
Adverse event, non-fatal	5	5
Subject decision	-	1
Study Terminated by the Sponsor	3	4

Baseline characteristics

Reporting groups

Reporting group title	Ruxolitinib plus Capecitabine
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Reporting group description:

Ruxolitinib 15 mg in combination with a starting dose of Capecitabine 2000 mg/m² administered orally twice daily (BID).

Reporting group title	Placebo Plus Capecitabine
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Reporting group description:

Placebo tablets in combination with a starting dose of Capecitabine 2000 mg/m².

Reporting group values	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine	Total
Number of subjects	43	43	86
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	12	28
From 65-84 years	26	30	56
85 years and over	1	1	2
Age continuous			
Units: years			
arithmetic mean	65.4	68.8	
standard deviation	± 10.63	± 8.43	-
Gender categorical			
Units: Subjects			
Female	18	21	39
Male	25	22	47

End points

End points reporting groups

Reporting group title	Ruxolitinib plus Capecitabine
Reporting group description:	Ruxolitinib 15 mg in combination with a starting dose of Capecitabine 2000 mg/m ² administered orally twice daily (BID).
Reporting group title	Placebo Plus Capecitabine
Reporting group description:	Placebo tablets in combination with a starting dose of Capecitabine 2000 mg/m ² .

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	Overall survival is reported here based on the number of days from randomization to death or until the data cut-off.
End point type	Primary
End point timeframe:	Randomization until death due to any cause up to 6-months or to the data cutoff 11FEB2016.

End point values	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 ^[1]	43 ^[2]		
Units: Days				
median (confidence interval 95%)	108.0 (62.0 to 124.0)	149.0 (84.0 to 256.0)		

Notes:

- [1] - The intent-to-treat (ITT) population consisted of all participants randomized to the study.
[2] - The intent-to-treat (ITT) population consisted of all participants randomized to the study.

Statistical analyses

Statistical analysis title	Overall Survival (OS)
Comparison groups	Ruxolitinib plus Capecitabine v Placebo Plus Capecitabine
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.584
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.886
upper limit	2.83

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
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End point description:

PFS is defined as the number of days from randomization until the earliest date of disease progression determined by investigator assessment of objective radiographic disease assessments per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, or death due to any cause if sooner. Progressive Disease (PD) is defined using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as at least a 20% increase in the sum of the Longest Diameter (LD) of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions or unequivocal progression of non-target lesions.

End point type	Secondary
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End point timeframe:

Randomization to disease progression, or death due to any cause if sooner; up to 6-months or to the data cutoff 11FEB2016.

End point values	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 ^[3]	43 ^[4]		
Units: Days				
median (confidence interval 95%)	48 (37 to 83)	61 (41 to 86)		

Notes:

[3] - ITT population

[4] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
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End point description:

Objective response rate determined by radiographic disease assessments per Response Evaluation Criteria in Solid Tumours RECIST (v1.1), by investigator assessment and was defined as the percentage of participants with Complete Response (CR) or Partial Response (PR) by RECIST at any post baseline visit. Per RECIST for target lesions and assessed by computed tomography (CT) and/or magnetic resonance imaging (MRI): Complete Response (CR), Disappearance of all target and non-target lesions and no appearance of new lesions; Partial Response (PR), $\geq 30\%$ decrease in the sum of the longest diameter of target lesions with no worsening of non-target lesions and no new lesions; Overall Response (OR) = CR + PR.

End point type	Secondary
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End point timeframe:

Baseline through end of study; up to 6-months or to the data cutoff 11FEB2016.

End point values	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 ^[5]	43 ^[6]		
Units: Percentage of participants				
number (not applicable)				
Objective response	4.7	2.3		
Complete response	2.3	0		
Partial response	2.3	2.3		

Notes:

[5] - ITT population

[6] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response
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End point description:

Duration of overall response was defined as the time in months from Complete Response (CR) or Partial Response (PR) by Response Evaluation Criteria in Solid Tumours (RECIST v1.1) until the first date Progressive Disease (PD) was objectively documented or until the date of death. Per RECIST for target lesions and assessed by computed tomography (CT) and/or magnetic resonance imaging (MRI): Complete Response (CR), Disappearance of all target and non-target lesions and no appearance of new lesions; Partial Response (PR), $\geq 30\%$ decrease in the sum of the longest diameter of target lesions with no worsening of non-target lesions and no new lesions; Overall Response (OR) = CR + PR.

End point type	Secondary
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End point timeframe:

Baseline through end of study; up to 6-months or to the data cutoff 11FEB2016.

End point values	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 ^[7]	43 ^[8]		
Units: Days				
median (confidence interval 95%)	999.99 (999.99 to 999.99)	999.99 (999.99 to 999.99)		

Notes:

[7] - DOR was not evaluable in the treatment group due to the insufficient number of subjects with events.

[8] - DOR was not evaluable in the treatment group due to the insufficient number of subjects with events.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study medication through the double-blind period through 30 days post-study termination up to 6-months or to the data cutoff 13APR2016.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Ruxolitinib plus Capecitabine
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Reporting group description:

Ruxolitinib 15 mg in combination with a starting dose of Capecitabine 2000 mg/m² administered orally twice daily (BID).

Reporting group title	Placebo Plus Capecitabine
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Reporting group description:

Placebo tablets in combination with a starting dose of Capecitabine 2000 mg/m².

Serious adverse events	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 42 (71.43%)	21 / 43 (48.84%)	
number of deaths (all causes)	31	31	
number of deaths resulting from adverse events	8	2	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gait disturbance			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 42 (2.38%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sudden cardiac death			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sudden death			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Early satiety			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 42 (9.52%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 42 (4.76%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Blood bilirubin increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (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	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			

subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 42 (0.00%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 42 (4.76%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 42 (4.76%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 42 (9.52%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	4 / 42 (9.52%)	3 / 43 (6.98%)	
occurrences causally related to treatment / all	1 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 42 (2.38%)	4 / 43 (9.30%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric stenosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			

subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	2 / 42 (4.76%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
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	1 / 42 (2.38%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 42 (4.76%)	3 / 43 (6.98%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
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	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
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	Ruxolitinib plus Capecitabine	Placebo Plus Capecitabine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 42 (90.48%)	41 / 43 (95.35%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 42 (9.52%)	1 / 43 (2.33%)	
occurrences (all)	4	1	
Hypotension			
subjects affected / exposed	0 / 42 (0.00%)	5 / 43 (11.63%)	
occurrences (all)	0	5	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	10 / 42 (23.81%)	15 / 43 (34.88%)	
occurrences (all)	11	15	
Oedema peripheral			
subjects affected / exposed	7 / 42 (16.67%)	8 / 43 (18.60%)	
occurrences (all)	8	8	
Asthenia			
subjects affected / exposed	7 / 42 (16.67%)	4 / 43 (9.30%)	
occurrences (all)	7	5	
Chills			
subjects affected / exposed	4 / 42 (9.52%)	2 / 43 (4.65%)	
occurrences (all)	4	2	
Chest pain			
subjects affected / exposed	3 / 42 (7.14%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Malaise			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Pain			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Oedema			
subjects affected / exposed	3 / 42 (7.14%)	2 / 43 (4.65%)	
occurrences (all)	3	3	
Pyrexia			
subjects affected / exposed	8 / 42 (19.05%)	6 / 43 (13.95%)	
occurrences (all)	9	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 42 (2.38%)	4 / 43 (9.30%)	
occurrences (all)	1	4	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 42 (9.52%)	1 / 43 (2.33%)	
occurrences (all)	5	1	
Depression			

subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 3	1 / 43 (2.33%) 1	
Insomnia subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	3 / 43 (6.98%) 3	
Investigations Blood bilirubin increased subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 3	3 / 43 (6.98%) 3	
Weight decreased subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 3	4 / 43 (9.30%) 4	
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	3 / 43 (6.98%) 4	
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	3 / 43 (6.98%) 3	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	4 / 43 (9.30%) 6	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	6 / 42 (14.29%) 7	4 / 43 (9.30%) 4	
Headache subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2	3 / 43 (6.98%) 3	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	17 / 42 (40.48%) 18	10 / 43 (23.26%) 14	
Leukocytosis subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	3 / 43 (6.98%) 3	

Leukopenia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Neutropenia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	4	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	13 / 42 (30.95%)	4 / 43 (9.30%)	
occurrences (all)	15	4	
Nausea			
subjects affected / exposed	10 / 42 (23.81%)	10 / 43 (23.26%)	
occurrences (all)	10	12	
Vomiting			
subjects affected / exposed	12 / 42 (28.57%)	10 / 43 (23.26%)	
occurrences (all)	15	10	
Diarrhoea			
subjects affected / exposed	12 / 42 (28.57%)	11 / 43 (25.58%)	
occurrences (all)	17	17	
Abdominal distension			
subjects affected / exposed	12 / 42 (28.57%)	4 / 43 (9.30%)	
occurrences (all)	13	4	
Constipation			
subjects affected / exposed	9 / 42 (21.43%)	12 / 43 (27.91%)	
occurrences (all)	10	12	
Ascites			
subjects affected / exposed	5 / 42 (11.90%)	5 / 43 (11.63%)	
occurrences (all)	5	5	
Stomatitis			
subjects affected / exposed	6 / 42 (14.29%)	4 / 43 (9.30%)	
occurrences (all)	6	4	
Abdominal pain upper			
subjects affected / exposed	6 / 42 (14.29%)	4 / 43 (9.30%)	
occurrences (all)	7	4	
Flatulence			

subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 4	1 / 43 (2.33%) 1	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	11 / 42 (26.19%)	11 / 43 (25.58%)	
occurrences (all)	14	13	
Skin hyperpigmentation			
subjects affected / exposed	4 / 42 (9.52%)	0 / 43 (0.00%)	
occurrences (all)	6	0	
Dry skin			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 42 (7.14%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 42 (7.14%)	7 / 43 (16.28%)	
occurrences (all)	3	7	
Muscular weakness			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	3	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 42 (26.19%)	12 / 43 (27.91%)	
occurrences (all)	11	15	
Hypokalaemia			
subjects affected / exposed	8 / 42 (19.05%)	9 / 43 (20.93%)	
occurrences (all)	8	11	
Dehydration			

subjects affected / exposed	4 / 42 (9.52%)	3 / 43 (6.98%)
occurrences (all)	5	3
Hyponatraemia		
subjects affected / exposed	5 / 42 (11.90%)	2 / 43 (4.65%)
occurrences (all)	5	2
Hyperglycaemia		
subjects affected / exposed	3 / 42 (7.14%)	6 / 43 (13.95%)
occurrences (all)	3	7
Hypoalbuminaemia		
subjects affected / exposed	1 / 42 (2.38%)	5 / 43 (11.63%)
occurrences (all)	1	5
Hypophosphataemia		
subjects affected / exposed	1 / 42 (2.38%)	3 / 43 (6.98%)
occurrences (all)	1	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 September 2014	The primary purpose of the amendment was to clarify eligibility criteria and the capecitabine treatment regimen to require that only 500 mg Capecitabine tablets be dispensed because of intersubject dose variability concerns associated with administering 2 different tablet strengths (150 mg and 500 mg).
25 January 2016	The primary purpose of the amendment was to address the Medicines and Healthcare products Regulatory Agency (MHRA) 19 JAN 2016 Grounds for Non Acceptance.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 February 2016	The study was terminated prior to the final analysis at the recommendation of the Data Monitoring Committee based on the review of efficacy in the 18424-362 (JANUS 1).	-

Notes:

Limitations and caveats

None reported