



Clinical trial results:

A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Gemcitabine and Nab-paclitaxel combined with Momelotinib in Subjects with Previously Untreated Metastatic Pancreatic Ductal Adenocarcinoma Preceded by a Dose-finding, Lead-in Phase Summary

EudraCT number	2014-004480-20
Trial protocol	HU DE ES GB CZ IT
Global end of trial date	10 April 2017

Results information

Result version number	v1
This version publication date	22 April 2018
First version publication date	22 April 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-370-1296
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02101021
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences International Ltd., GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences International Ltd., GileadClinicalTrials@gilead.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	10 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2017
Global end of trial reached?	Yes
Global end of trial date	10 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

There were two planned phases to this study. The lead-in phase evaluated the safety, pharmacokinetics, and define the maximum tolerated dose (MTD) of momelotinib (MMB) combined with nab-paclitaxel and gemcitabine (nab-P + G) in adults with previously untreated metastatic pancreatic ductal adenocarcinoma. The primary objectives of the randomized treatment phase were to evaluate the efficacy, safety, and tolerability of nab-P + G with either MMB administered at the MTD or placebo in adults with previously untreated metastatic pancreatic ductal adenocarcinoma. Participants were to continue study treatment until disease progression, unacceptable toxicity, consent withdrawal, or participant's refusal of treatment. Following treatment, participants were to be followed for safety for 30 days and for survival approximately every 3 months for up to 3 years.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	25
EEA total number of subjects	0

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)	16
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States (US). The first participant was screened on 02 June 2014. The last study visit occurred on 10 April 2017.

Pre-assignment

Screening details:

38 participants were screened.

Data submitted represent analysis performed on data collected in the lead-in phase by the Study Termination Date, 10 April 2017. The study was discontinued before initiation of the randomized treatment phase, therefore no data were collected for the randomized treatment phase.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MMB Dose Level 1

Arm description:

Momelotinib (MMB) 100 mg tablet once daily + albumin-bound (nab)-paclitaxel plus gemcitabine (nab-P+G) (1000+1000 mg/m²) intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle

Arm type	Experimental
Investigational medicinal product name	Momelotinib 100 mg
Investigational medicinal product code	
Other name	GS-0387, CYT387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg oral tablet (s)

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Arm title	MMB Dose Level 2
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Arm description:

MMB 150 mg tablet once daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Arm type	Experimental
Investigational medicinal product name	Momelotinib 150 mg
Investigational medicinal product code	
Other name	GS-0387, CYT387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg oral tablet (s)

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Arm title	MMB Dose Level 3
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Arm description:

MMB 200 mg tablet once daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Arm type	Experimental
Investigational medicinal product name	Momelotinib 200 mg
Investigational medicinal product code	
Other name	GS-0387, CYT387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg oral tablet (s)

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Arm title	MMB Dose Level 4
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Arm description:

MMB 150 mg tablet twice daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of

each 28-day cycle

Arm type	Experimental
Investigational medicinal product name	Momelotinib 150 mg
Investigational medicinal product code	
Other name	GS-0387, CYT387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg oral tablet (s)

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Arm title	MMB Dose Level 5
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Arm description:

MMB 200 mg tablet twice daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Arm type	Experimental
Investigational medicinal product name	Momelotinib 200 mg
Investigational medicinal product code	
Other name	GS-0387, CYT387
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg oral tablet (s)

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m² administered over approximately 30 to 40 minutes

Number of subjects in period 1	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3
Started	7	4	7
Completed	0	0	0
Not completed	7	4	7
Withdrew Consent from study	1	1	-
Death	4	3	6
Study Terminated by Sponsor	1	-	1
Lost to follow-up	1	-	-

Number of subjects in period 1	MMB Dose Level 4	MMB Dose Level 5
Started	3	4
Completed	0	0
Not completed	3	4
Withdrew Consent from study	2	-
Death	-	3
Study Terminated by Sponsor	1	1
Lost to follow-up	-	-

Baseline characteristics

Reporting groups

Reporting group title	MMB Dose Level 1
Reporting group description: Momelotinib (MMB) 100 mg tablet once daily + albumin-bound (nab)-paclitaxel plus gemcitabine (nab-P+G) (1000+1000 mg/m ²) intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 2
Reporting group description: MMB 150 mg tablet once daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 3
Reporting group description: MMB 200 mg tablet once daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 4
Reporting group description: MMB 150 mg tablet twice daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 5
Reporting group description: MMB 200 mg tablet twice daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	

Reporting group values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3
Number of subjects	7	4	7
Age categorical Units: Subjects			
Age continuous			
All Enrolled Analysis Set: all participants who received a study participant identification number in the study after screening.			
Units: years arithmetic mean standard deviation	59.9 ± 12.32	63.5 ± 12.12	64.7 ± 8.79
Gender categorical Units: Subjects			
Female	2	3	2
Male	5	1	5
Race Units: Subjects			
Asian	0	0	1
White	6	3	6
Other	1	1	0
Ethnicity Units: Subjects			

Hispanic or Latino	1	0	0
Not Hispanic or Latino	6	4	7

Reporting group values	MMB Dose Level 4	MMB Dose Level 5	Total
Number of subjects	3	4	25
Age categorical Units: Subjects			

Age continuous			
All Enrolled Analysis Set: all participants who received a study participant identification number in the study after screening.			
Units: years arithmetic mean standard deviation	52.0 ± 5.00	59.0 ± 9.13	-
Gender categorical Units: Subjects			
Female	0	1	8
Male	3	3	17
Race Units: Subjects			
Asian	0	0	1
White	3	4	22
Other	0	0	2
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	3	4	24

End points

End points reporting groups

Reporting group title	MMB Dose Level 1
Reporting group description: Mometotinib (MMB) 100 mg tablet once daily + albumin-bound (nab)-paclitaxel plus gemcitabine (nab-P+G) (1000+1000 mg/m ²) intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 2
Reporting group description: MMB 150 mg tablet once daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 3
Reporting group description: MMB 200 mg tablet once daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 4
Reporting group description: MMB 150 mg tablet twice daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	
Reporting group title	MMB Dose Level 5
Reporting group description: MMB 200 mg tablet twice daily + nab-P+G (1000+1000 mg/m ²) IV infusion on Days 1, 8, and 15 of each 28-day cycle	

Primary: Lead-In Phase: Percentage of Participants Experiencing Treatment-Emergent Dose Limiting Toxicity (DLT) Adverse Events

End point title	Lead-In Phase: Percentage of Participants Experiencing Treatment-Emergent Dose Limiting Toxicity (DLT) Adverse Events ^[1]
End point description: Dose limiting toxicities were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Dose limiting toxicities referred to toxicities experienced during the first 28 days (Cycle 1) of treatment that were judged to be clinically significant and related to study treatment. DLT-Evaluable Analysis Set: participants in the Safety Analysis Set who completed all treatment and safety procedures through Day 28, inclusive, or experienced a DLT prior to Day 29. Participants in the DLT-Evaluable Analysis Set with available data were analyzed.	
End point type	Primary
End point timeframe: Up to 28 Days	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analysis was planned or performed.	

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	6	3
Units: percentage of participants				
number (not applicable)	16.7	0	16.7	0

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Randomized Treatment Phase: Overall Survival (OS)

End point title	Randomized Treatment Phase: Overall Survival (OS) ^[2]
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End point description:

End point type	Primary
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End point timeframe:

Baseline up to the Date of Death or Censoring

Notes:

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

Justification: No statistical analysis was performed because the study was discontinued prior to initiation of randomized phase.

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[3]	0 ^[4]	0 ^[5]	0 ^[6]
Units: Months				
median (inter-quartile range (Q1-Q3))	(to)	(to)	(to)	(to)

Notes:

[3] - The study was discontinued before initiation of the randomized treatment phase.

[4] - The study was discontinued before initiation of the randomized treatment phase.

[5] - The study was discontinued before initiation of the randomized treatment phase.

[6] - The study was discontinued before initiation of the randomized treatment phase.

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[7]			
Units: Months				
median (inter-quartile range (Q1-Q3))	(to)			

Notes:

[7] - The study was discontinued before initiation of the randomized treatment phase.

Statistical analyses

No statistical analyses for this end point

Secondary: Lead-In Phase: Overall Survival (OS)

End point title	Lead-In Phase: Overall Survival (OS)
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End point description:

Overall survival was defined as the time interval from first dose date of MMB to death from any cause.

Participants in the All Enrolled Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Baseline up to the Date of Death or Censoring

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	7	3
Units: Months				
median (inter-quartile range (Q1-Q3))	12.4 (3.9 to 22.2)	5.1 (3.7 to 11.3)	8.7 (7.3 to 18.3)	5.6 (4.8 to 18.1)

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Months				
median (inter-quartile range (Q1-Q3))	7.1 (5.9 to 12.0)			

Statistical analyses

Statistical analysis title	OS- Comparison of Groups
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Comparison groups	MMB Dose Level 1 v MMB Dose Level 2 v MMB Dose Level 3 v MMB Dose Level 4 v MMB Dose Level 5
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Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other ^[8]
Parameter estimate	Median OS in Months
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	18.8

Notes:

[8] - Medians of OS with 95% confidence intervals (CI) were derived using Kaplan-Meier (KM) method. 16 participants (64.0%) died during the study.

Secondary: Lead-In Phase: Progression-Free Survival (PFS)

End point title	Lead-In Phase: Progression-Free Survival (PFS)
End point description:	Progression-free survival was defined as the time interval from the first dose of MMB to the earlier of the first documentation of definitive disease progression or death from any cause. Participants in the All Enrolled Analysis Set were analyzed.
End point type	Secondary
End point timeframe:	Baseline up to the Date of Event or Censoring

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	7	3
Units: Months				
median (inter-quartile range (Q1-Q3))	5.3 (1.4 to 7.4)	3.2 (1.9 to 4.8)	5.5 (5.3 to 7.2)	5.3 (0.0 to 13.0)

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Months				
median (inter-quartile range (Q1-Q3))	5.5 (4.5 to 10.1)			

Statistical analyses

Statistical analysis title	PFS- Comparison of Groups
Comparison groups	MMB Dose Level 1 v MMB Dose Level 2 v MMB Dose Level 3 v MMB Dose Level 4 v MMB Dose Level 5

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other ^[9]
Parameter estimate	Median PFS in Months
Point estimate	5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	7.2

Notes:

[9] - Medians of PFS with 95% CIs were derived using Kaplan-Meier (KM) method. 17 participants (68.0%) experienced documented events of progressive disease (PD) (13 participants [52.0%]) or death (4 participants [16.0%]). T

Secondary: Lead-In Phase: Overall Response Rate (ORR)

End point title	Lead-In Phase: Overall Response Rate (ORR)
End point description:	The ORR was defined as the proportion of participants who achieved a best overall response (BOR) during MMB therapy of complete response (CR) or partial response (PR). Participants in the All Enrolled Analysis Set were analyzed.
End point type	Secondary
End point timeframe:	Baseline up to the Last Tumor Assessment Date

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	7	3
Units: participants				
Complete Response (CR)	2	1	3	1
Partial Response (PR)	2	2	4	1

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants				
Complete Response (CR)	0			
Partial Response (PR)	4			

Statistical analyses

Statistical analysis title	ORR- Comparison of Groups
Comparison groups	MMB Dose Level 1 v MMB Dose Level 2 v MMB Dose Level 3 v MMB Dose Level 4 v MMB Dose Level 5

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other ^[10]
Parameter estimate	Percentage ORR
Point estimate	28
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.1
upper limit	49.4

Notes:

[10] - ORR were presented with corresponding 2-sided 95% exact CIs based on the Clopper-Pearson method.

Secondary: Randomized Treatment Phase: Progression-Free Survival (PFS)

End point title	Randomized Treatment Phase: Progression-Free Survival (PFS)
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to the Date of Event or Censoring	

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[11]	0 ^[12]	0 ^[13]	0 ^[14]
Units: Months				
median (inter-quartile range (Q1-Q3))	(to)	(to)	(to)	(to)

Notes:

[11] - The study was discontinued before initiation of the randomized treatment phase.

[12] - The study was discontinued before initiation of the randomized treatment phase.

[13] - The study was discontinued before initiation of the randomized treatment phase.

[14] - The study was discontinued before initiation of the randomized treatment phase.

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[15]			
Units: Months				
median (inter-quartile range (Q1-Q3))	(to)			

Notes:

[15] - The study was discontinued before initiation of the randomized treatment phase.

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Treatment Phase: Overall Response Rate (ORR)

End point title	Randomized Treatment Phase: Overall Response Rate (ORR)
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to the Last Tumor Assessment Date

End point values	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3	MMB Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[16]	0 ^[17]	0 ^[18]	0 ^[19]
Units: participants				

Notes:

[16] - The study was discontinued before initiation of the randomized treatment phase.

[17] - The study was discontinued before initiation of the randomized treatment phase.

[18] - The study was discontinued before initiation of the randomized treatment phase.

[19] - The study was discontinued before initiation of the randomized treatment phase.

End point values	MMB Dose Level 5			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[20]			
Units: participants				

Notes:

[20] - The study was discontinued before initiation of the randomized treatment phase.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to the last dose date plus 30 days (maximum exposure= 63.7 weeks)

Adverse event reporting additional description:

Safety Analysis Set: all participants who were randomized and received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	MMB Dose Level 1
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Reporting group description:

Momelotinib (MMB) 100 mg tablet once daily + albumin-bound (nab)-paclitaxel plus gemcitabine (nab-P+G) (1000+1000 mg/m²) intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle

Reporting group title	MMB Dose Level 2
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Reporting group description:

MMB 150 mg tablet once daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Reporting group title	MMB Dose Level 3
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Reporting group description:

MMB 200 mg tablet once daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Reporting group title	MMB Dose Level 4
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Reporting group description:

MMB 150 mg tablet twice daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Reporting group title	MMB Dose Level 5
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Reporting group description:

MMB 200 mg tablet twice daily + nab-P+G (1000+1000 mg/m²) IV infusion on Days 1, 8, and 15 of each 28-day cycle

Serious adverse events	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	3 / 4 (75.00%)	5 / 7 (71.43%)
number of deaths (all causes)	4	3	6
number of deaths resulting from adverse events			
Investigations			
Weight decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Rib fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Embolic stroke			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	3 / 7 (42.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MMB Dose Level 4	MMB Dose Level 5	
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Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	4 / 4 (100.00%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events			
Investigations			
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Embolic stroke			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MMB Dose Level 1	MMB Dose Level 2	MMB Dose Level 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tumor pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	2 / 7 (28.57%)
occurrences (all)	2	1	2
Hypotension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Deep vein thrombosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Embolism venous			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Subclavian vein thrombosis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis limb			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 7 (71.43%)	3 / 4 (75.00%)	6 / 7 (85.71%)
occurrences (all)	5	6	7
Oedema peripheral			
subjects affected / exposed	4 / 7 (57.14%)	1 / 4 (25.00%)	2 / 7 (28.57%)
occurrences (all)	4	2	2
Pyrexia			
subjects affected / exposed	3 / 7 (42.86%)	2 / 4 (50.00%)	3 / 7 (42.86%)
occurrences (all)	3	3	4
Chills			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Malaise			
subjects affected / exposed	1 / 7 (14.29%)	2 / 4 (50.00%)	1 / 7 (14.29%)
occurrences (all)	1	2	1
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Face oedema			

subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Generalised oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Temperature intolerance			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	2 / 7 (28.57%)
occurrences (all)	1	1	2
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Epistaxis			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Alveolitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pulmonary oedema			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Respiratory distress			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	2 / 7 (28.57%)
occurrences (all)	2	1	2
Anxiety			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Personality change			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Sleep disorder subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1	0 / 7 (0.00%) 0
Investigations			
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 4 (25.00%) 1	1 / 7 (14.29%) 1
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	2 / 7 (28.57%) 2
Weight decreased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 2
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 3
Liver function test increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1	0 / 7 (0.00%) 0
Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Blood uric acid increased			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Troponin increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Urine output decreased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Injury, poisoning and procedural complications			
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1	0 / 7 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Head injury subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Joint injury subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Limb injury subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Transfusion reaction subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Cardiac disorders			
Tachycardia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	1 / 7 (14.29%) 2
Acute myocardial infarction			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Intracardiac mass			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	3 / 7 (42.86%)
occurrences (all)	3	0	4
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	3 / 7 (42.86%)
occurrences (all)	0	1	3
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 7 (42.86%)	1 / 4 (25.00%)	2 / 7 (28.57%)
occurrences (all)	4	1	2
Headache			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	3 / 7 (42.86%)
occurrences (all)	1	1	4
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Peripheral motor neuropathy			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Akathisia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dizziness exertional			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dizziness postural			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Extrapyramidal disorder			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Facial paresis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Peroneal nerve palsy subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	6 / 7 (85.71%) 6	2 / 4 (50.00%) 4	4 / 7 (57.14%) 4
Neutropenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 4 (25.00%) 2	1 / 7 (14.29%) 7
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Disseminated intravascular coagulation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Leukocytosis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Thrombocytosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Eye disorders			

Dry eye subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1	0 / 7 (0.00%) 0
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	5 / 7 (71.43%) 7	4 / 4 (100.00%) 5	4 / 7 (57.14%) 8
Diarrhoea subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3	3 / 4 (75.00%) 4	3 / 7 (42.86%) 5
Constipation subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	3 / 4 (75.00%) 3	3 / 7 (42.86%) 5
Vomiting subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 4	3 / 4 (75.00%) 5	4 / 7 (57.14%) 5
Abdominal pain subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	1 / 4 (25.00%) 1	3 / 7 (42.86%) 4
Dyspepsia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 4 (25.00%) 1	1 / 7 (14.29%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 4 (25.00%) 1	1 / 7 (14.29%) 1
Abdominal distension subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 4 (25.00%) 1	0 / 7 (0.00%) 0
Ascites subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Haematochezia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Abdominal tenderness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Duodenal ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ileus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Melaena			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pancreatic failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Paraesthesia oral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Stomatitis			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Varices oesophageal subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Hepatobiliary disorders			
Bile duct obstruction subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Biliary dilatation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Portal hypertension subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3	2 / 4 (50.00%) 2	3 / 7 (42.86%) 3
Rash subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	0 / 4 (0.00%) 0	3 / 7 (42.86%) 3
Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	2 / 7 (28.57%) 2
Rash macular subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Nail bed disorder subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Rash papular			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin hypopigmentation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nephrolithiasis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	3	0	1
Pain in extremity			

subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Muscle fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	3 / 7 (42.86%)
occurrences (all)	2	2	3
Oral candidiasis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	3 / 7 (42.86%)
occurrences (all)	1	0	4

Candida infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Bronchiolitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Endocarditis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pulmonary tuberculosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Soft tissue infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Viral infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1	0 / 7 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	2 / 4 (50.00%) 2	2 / 7 (28.57%) 4
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	2 / 4 (50.00%) 2	3 / 7 (42.86%) 3
Dehydration subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	3 / 7 (42.86%) 4
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	4 / 7 (57.14%) 5
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0	2 / 7 (28.57%) 2
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	2 / 7 (28.57%) 2
Hypoglycaemia subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0
Cachexia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1
Hyperkalaemia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypernatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Malnutrition			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Non-serious adverse events	MMB Dose Level 4	MMB Dose Level 5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	4 / 4 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Tumor pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
occurrences (all)	3	10	
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Embolism venous			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Venous thrombosis limb			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	4 / 4 (100.00%)	
occurrences (all)	2	6	
Oedema peripheral			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
occurrences (all)	2	3	
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 4 (75.00%)	
occurrences (all)	1	6	
Chills			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Early satiety			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Temperature intolerance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Cough			

subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	3
Epistaxis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	3
Hypoxia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	3
Dyspnoea exertional		
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	3
Alveolitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Dysphonia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Hiccups		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Nasal congestion		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Pleural effusion		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Pleuritic pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Pneumonitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Productive cough		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Pulmonary embolism		

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Respiratory distress			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Panic attack			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	

Personality change subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Sleep disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Investigations			
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 8	1 / 4 (25.00%) 2	
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 4 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 4 (0.00%) 0	
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Liver function test increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0	
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Blood creatinine increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 3	
Troponin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Urine output decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Injury, poisoning and procedural complications			
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Fall subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Head injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Joint injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Limb injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Transfusion reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Cardiac disorders			

Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Intracardiac mass			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 3 (66.67%)	2 / 4 (50.00%)	
occurrences (all)	2	2	
Neuropathy peripheral			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
occurrences (all)	2	3	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 3 (66.67%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Paraesthesia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Peripheral motor neuropathy		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Peripheral sensorimotor neuropathy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Akathisia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Balance disorder		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Cerebrovascular accident		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Cognitive disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Dizziness exertional		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Dizziness postural		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Dysaesthesia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Extrapyramidal disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Facial paresis		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Hemiparesis		

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Peroneal nerve palsy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
occurrences (all)	2	5	
Neutropenia			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
occurrences (all)	4	6	
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	
occurrences (all)	2	3	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Thrombocytosis			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 3	3 / 4 (75.00%) 8	
Diarrhoea subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 5	3 / 4 (75.00%) 4	
Constipation subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	3 / 4 (75.00%) 3	
Vomiting subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 4 (75.00%) 6	
Abdominal pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	3 / 4 (75.00%) 4	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Abdominal distension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Ascites			

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Haematochezia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Abdominal pain lower		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Abdominal tenderness		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Duodenal ulcer		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Gastritis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Gastrointestinal pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Ileus		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Melaena		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Pancreatic failure		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Paraesthesia oral		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Rectal haemorrhage		

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Small intestinal obstruction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Stomatitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Varices oesophageal subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0	
Hepatobiliary disorders Bile duct obstruction subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0	
Biliary dilatation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Portal hypertension subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 4 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 4 (50.00%) 2	
Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Rash macular subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Nail bed disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Skin hypopigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Muscular weakness			

subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	
occurrences (all)	1	2	
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Muscle fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			

Urinary tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Oral candidiasis		
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	0
Candida infection		
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)
occurrences (all)	1	1
Cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Pneumonia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Bronchiolitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Bronchitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Catheter site infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Ear infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Endocarditis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Gastroenteritis viral		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Oesophageal candidiasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0

Pulmonary tuberculosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Soft tissue infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Viral infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	1 / 4 (25.00%) 1	
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 4 (0.00%) 0	
Dehydration subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1	
Hypoglycaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cachexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Malnutrition			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 March 2014	The protocol was revised to address administrative changes and to respond to the clinical questions posted by the FDA on the Solid Tumor IND received by Gilead Sciences, Inc.
25 August 2014	The protocol was revised to specify stratification and eligibility criteria for the randomized phase and to incorporate new emerging risk and drug-drug interaction data.
16 February 2015	Biostatistical changes were made to the sample size in this protocol to enable this single study to serve as a registrational trial, if safety and effectiveness of the combination is demonstrated in support of a potential new drug application (NDA) for the frontline treatment of metastatic pancreatic cancer. An optional intensive pharmacokinetic (PK) substudy was also incorporated for evaluation of drugdrug interactions between MMB and nab-paclitaxel or gemcitabine as requested by the Agency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 April 2017	<p>Following internal review, Gilead Sciences, Inc. decided not to move forward into the randomized treatment phase of this study given the minimal treatment effect, the low likelihood of improved outcome in patients with pancreatic cancer, and a similar lack of efficacy reported in another Janus kinase (JAK) program for a similar indication. Gilead decided to discontinue the 3-year long-term survival follow-up period following completion of study treatment for all participants in the lead-in phase. The study was formally closed once all participants completed the 30-day safety follow-up visit.</p> <p>An Administrative Letter dated 11 April 2016 the decision not to initiate the randomized treatment phase was distributed to the European and non-European sites.</p>	-

Notes:

Limitations and caveats

None reported