Clinical trial results:
A Randomized Phase 2/3 Study of DACOGEN® (Decitabine) Plus Talacotuzumab (JNJ-56022473; Anti CD123) Versus DACOGEN (Decitabine) Alone in Patients with AML who are not Candidates for Intensive Chemotherapy

Summary

EudraCT number	2015-001611-12
Trial protocol	BE ES DE GB SE PL FR IT
Global end of trial date	25 January 2018

Results information

Result version number	v1 (current)
This version publication date	10 February 2019
First version publication date	10 February 2019

Trial information

Trial identification

Sponsor protocol code	56022473AML2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02472145
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920, Route 202 South,Raritan, NJ, United States, 08869
Public contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 January 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this trial were to assess safety and to confirm the recommended Phase 2 dose (RP2D) of talacotuzumab monotherapy (Part A) and to assess the complete response (CR) rate and overall survival (OS) in subjects with previously untreated acute myeloid leukemia (AML) who were not eligible for intense induction chemotherapy and who were randomly assigned to receive decitabine plus talacotuzumab at the RP2D or decitabine alone (Part B).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety assessment was based on reported adverse events (AE), clinical laboratory tests, vital sign measurements, physical examinations, electrocardiogram (ECG) findings, and Eastern Cooperative Oncology Group (ECOG) performance status.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Poland: 24
Country: Number of subjects enrolled	Russian Federation: 56
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Turkey: 7
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	United States: 26
Country: Number of subjects enrolled	Australia: 28
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Spain: 43

Worldwide total number of subjects	326
EEA total number of subjects	156

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)	4
From 65 to 84 years	305
85 years and over	17

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

326 subjects enrolled (10-Part A,316-Part B[159 in decitabine arm,157 in decitabine+JNJ-56022473 arm]), all subjects discontinued study. Safety: Part A- 10, Part B(Decitabine)- 165(9 who received decitabine, not JNJ-56022473 included, 3 untreated excluded),Part B(Decitabine+JNJ-56022473)-147 subjects(1 untreated,9 who received decitabine excluded).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Decitabine + JNJ-56022473

Arm description:

Subjects received 1 dose of JNJ-56022473 (talacotuzumab) at 9 milligram per kilogram (mg/kg) as intravenous (IV) infusion on Day 1 of cycle 1. From cycle 2 onwards, subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	DACOGEN
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Decitabine at a dose of 20 mg/m^2 IV on Days 1 to 5 of each 28-day cycle until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Investigational medicinal product name	JNJ-56022473
Investigational medicinal product code	
Other name	Talacotuzumab, Anti CD123
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 1 dose of JNJ-56022473 at 9 mg/kg as IV infusion on Day 1 of cycle 1 and on Day 8 and Day 22 of a 28-day cycle from cycle 2 onwards until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Arm title	Part B: Decitabine (Alone)

Arm description:

Subjects received decitabine 20 mg/m^2 on Days 1 to 5 of each 28-day cycle until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Arm type	Active comparator

Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	DACOGEN
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received decitabine 20 mg/m^2 IV administered daily on Days 1 to 5 of each 28-day cycle from cycle 2 onwards until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Arm title	Part B: Decitabine + JNJ-56022473

Arm description:

Subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	DACOGEN
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Decitabine at a dose of 20 mg/m^2 IV on Days 1 to 5 of each 28-day cycle onwards until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Investigational medicinal product name	JNJ-56022473
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received JNJ-56022473 at 9 mg/kg as IV infusion on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Number of subjects in period 1	Part A: Decitabine + JNJ-56022473	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473
Started	10	159	157
Treated	10	156	156
Completed	0	0	0
Not completed	10	159	157
Consent withdrawn by subject	-	9	13
Death	10	101	99
Unspecified	-	45	43
Sponsor decision	-	3	2
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Decitabine + JNJ-56022473
Reporting group description:	
Subjects received 1 dose of JNJ-56022473 (talacotuzumab) at 9 milligram per kilogram (mg/kg) as intravenous (IV) infusion on Day 1 of cycle 1. From cycle 2 onwards, subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.	
Reporting group title	Part B: Decitabine (Alone)
Reporting group description:	
Subjects received decitabine 20 mg/m^2 on Days 1 to 5 of each 28-day cycle until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.	
Reporting group title	Part B: Decitabine + JNJ-56022473
Reporting group description:	
Subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.	

Reporting group values	Part A: Decitabine + JNJ-56022473	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473
Number of subjects	10	159	157
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	0	0
From 65 to 84 years	6	148	151
85 years and over	0	11	6
Title for AgeContinuous			
Units: years			
arithmetic mean	65.4	75	75.2
standard deviation	± 10.88	± 5.6	± 5.32
Title for Gender			
Units: subjects			
Female	4	68	77
Male	6	91	80

Reporting group values	Total		
Number of subjects	326		
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	4		
From 65 to 84 years	305		
85 years and over	17		

Title for AgeContinuous Units: years arithmetic mean standard deviation	- 		
Title for Gender Units: subjects			
Female	149		
Male	177		

End points

End points reporting groups

Reporting group title	Part A: Decitabine + JNJ-56022473

Reporting group description:

Subjects received 1 dose of JNJ-56022473 (talacotuzumab) at 9 milligram per kilogram (mg/kg) as intravenous (IV) infusion on Day 1 of cycle 1. From cycle 2 onwards, subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.

Reporting group title	Part B: Decitabine (Alone)

Reporting group description:

Subjects received decitabine 20 mg/m^2 on Days 1 to 5 of each 28-day cycle until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Reporting group title	Part B: Decitabine + JNJ-56022473

Reporting group description:

Subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.

Primary: Part B: Percentage of Subjects who Achieved Complete Response (Complete Response Rate) Based on Investigator Assessment

End point title	Part B: Percentage of Subjects who Achieved Complete Response (Complete Response Rate) Based on Investigator Assessment[1]

End point description:

Complete response rate defined as percentage of subjects who achieved complete response as per modified International Working Group (IWG) criteria. CR: Bone marrow blasts less than (<)5 percent (%); absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count greater than (>)1.0*10^9/liter (L) (1000/micro liter [mcL]); platelet count >100*10^9/L (100 000/mcL); independence of red cell transfusions. Intent-to-Treat (ITT) population is defined as all randomized subjects, grouped per treatment assigned by randomization, regardless of the actual treatment received. This endpoint is reported here for Part B only as per the planned analysis.

End point type	Primary

End point timeframe:

Approximately up to 2.5 years

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	157		
Units: Percentage of subjects				
number (not applicable)	11.9	16.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Part B: Decitabine + JNJ-56022473 v Part B: Decitabine (Alone)
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4747
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2.8

Primary: Part B: Overall Survival

End point title	Part B: Overall Survival[2]

End point description:

Overall Survival (OS) was defined as the time from the date of randomization to date of death from any cause. Median Overall Survival was estimated by using the Kaplan-Meier method. ITT population is defined as all randomized subjects, grouped per treatment assigned by randomization, regardless of the actual treatment received. This endpoint is reported here for Part B only as per the planned analysis.

End point type	Primary

End point timeframe:

Approximately up to 2.5 years

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	157		
Units: Months				
median (confidence interval 95%)	7.26 (6.47 to 8.64)	5.36 (4.27 to 7.95)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Part B: Decitabine + JNJ-56022473 v Part B: Decitabine (Alone)

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7817
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.37

Secondary: Part B: Event-free Survival (EFS) Based on Investigator Assessment

End point title	Part B: Event-free Survival (EFS) Based on Investigator Assessment[3]

End point description:

EFS:time from randomization to treatment failure(TF),relapse from CR/CRi, death from any cause, whichever occurs first,per modified IWG criteria. TF:>25% absolute increase in bone marrow blast count from baseline to present assessment (20%-46%) on bone marrow aspirate or biopsy in case of dry tap; Relapse:Bone marrow blasts >=5%; reappearance of blasts in blood; development of extramedullary disease (ED); CR:Bone marrow blasts <5 %; absence of blasts with Auer rods(AR); absence of extramedullary disease; absolute neutrophil count>1.0*10^9/L(1000/mcL);platelet count>100*10^9/L(100 000/mcL);independence of red cell transfusions; CRi:Bone marrow blasts <5%; absence of blasts with AR; absence of ED; residual neutropenia <1.0*10^9/L(1000/mcL), thrombocytopenia<100*10^9/L(100 000/mcL);independence of red cell transfusions. ITT: all randomized subjects,grouped per treatment assigned by randomization, regardless treatment received. Endpoint is reported here for Part B per planned analysis.

End point type	Secondary

End point timeframe:

Approximately up to 2.5 years

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	157		
Units: Months				
median (confidence interval 95%)	6.24 (4.96 to 6.83)	4.50 (3.61 to 6.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Subjects who Achieved CR and CRi (Overall Response Rate)

End point title	Part B: Percentage of Subjects who Achieved CR and CRi (Overall Response Rate)[4]

End point description:

The Percentage of subjects who achieved CR and CRi, as per modified IWG criteria. CR: Bone marrow blasts less than (<)5 %; absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count greater than (>)1.0 *10^9/liter (L) (1000/ mcL); platelet count >100 *10^9/L (100 000/mcL); independence of red cell transfusions. CRi: Bone marrow blasts <5 %; absence of blasts with Auer rods; absence of extramedullary disease; residual neutropenia <1.0*10^9/L (1000/mcL) or thrombocytopenia <100*10^9/L (100 000/mcL); independence of red cell transfusions. ITT population: all randomized subjects, grouped per treatment assigned by randomization, regardless of actual treatment received. The Endpoint is reported here for Part B only as per planned analysis.

End point type	Secondary

End point timeframe:

Approximately up to 2.5 years

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	157		
Units: Percentage of subjects				
number (not applicable)	20.1	26.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Subjects With Complete Response (CR) Plus Minimal Residual Disease (MRD) Negative Complete Response With Incomplete Recovery (CRi)

End point title	Part B: Percentage of Subjects With Complete Response (CR) Plus Minimal Residual Disease (MRD) Negative Complete Response With Incomplete Recovery (CRi)[5]

End point description:

Percentage of subjects who achieved CR plus MRD-negative CRi were reported. MRD negativity defined as <1 blast or leukemic stem cell in 10,000 leukocytes (MRD level <10^4).CR: Bone marrow blasts less than (<)5 percent (%); absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count greater than (>)1.0*10^9/liter (L) (1000/mcL); platelet count >100*10^9/L (100 000/mcL); independence of red cell transfusions. CRi: Bone marrow blasts <5 %; absence of blasts with Auer rods; absence of extramedullary disease; residual neutropenia <1.0*10^9/L (1000/mcL) or thrombocytopenia <100*10^9/L (100 000/mcL); independence of red cell transfusions. Population included subjects in ITT, among whom MRD negativity was evaluated upon achieving response. This endpoint is reported here for Part B only as per the planned analysis.

End point type	Secondary

End point timeframe:

Approximately 2.5 years

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: Percentage of subjects				
number (not applicable)	13.8	21.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Time to Best Response

End point title	Part B: Time to Best Response[6]

End point description:

Time to best response is calculated as the time from the randomization date to the first documented date for the best response for subjects who achieved CR or CRi, as per modified IWG criteria. CR: Bone marrow blasts less than (<)5 %; absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count greater than (>)1.0 *10^9/liter (L) (1000/mcL); platelet count >100*10^9/L (100 000/mcL); independence of red cell transfusions; CRi: Bone marrow blasts <5 %; absence of blasts with Auer rods; absence of extramedullary disease; residual neutropenia <1.0*10^9/L (1000/mcL) or thrombocytopenia <100*10^9/L (100 000/mcL); independence of red cell transfusions. Population included subjects in ITT, who achieved CR or CRi. This endpoint is reported here for Part B only as per the planned analysis.

End point type	Secondary

End point timeframe:

Approximately 2.5 years

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	42		
Units: Weeks				
median (full range (min-max))	16.71 (7.1 to 41.6)	18.14 (7.3 to 68.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Duration of Best Response (DOR) Based on Investigator Assessment

End point title	Part B: Duration of Best Response (DOR) Based on Investigator Assessment[7]

End point description:

DOR: number of weeks from documented best response (CR/CRi) who achieved CR/CRi to relapse,

death due to relapse, date of censoring. Per modified IWG criteria: CR: Bone marrow blasts <5 %; absence of blasts with Auer rods; absence of extramedullary disease;absolute neutrophil count>1.0*10^9/L(1000/ mcL);platelet count >100*10^9/L (100 000/mcL);independence of red cell transfusions; CRi:Bone marrow blasts <5 %; absence of blasts with Auer rods; absence of extramedullary disease;residual neutropenia <1.0*10^9/L(1000/mcL) or thrombocytopenia <100*10^9/L(100 000/mcL);independence of red cell transfusions. "99999" indicates Median (Decitabine+JNJ-56022473 arm) and upper limit of 95% CI(Decitabine and Decitabine+JNJ-56022473 arm) was not estimable due to insufficient number of events. ITT population, who achieved CR or CRi. Endpoint reported is for Part B as per planned analysis.

End point type	Secondary

End point timeframe:

Approximately 2.5 years

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be reported for the specified arms only.

End point values	Part B: Decitabine (Alone)	Part B: Decitabine + JNJ-56022473		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	42		
Units: Weeks				
median (confidence interval 95%)	23.71 (15.43 to 99999)	99999 (29.86 to 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 2.5 years

Adverse event reporting additional description:

Safety Population defined as randomized subjects who received at least one dose of study medication, grouped according to actual treatment received (9 subjects from decitabine + JNJ-56022473 arm were grouped in the decitabine alone arm as they received only decitabine and not JNJ 56022473).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Part A: Decitabine + JNJ-56022473

Reporting group description:

Subjects received 1 dose of JNJ-56022473 (talacotuzumab) at 9 milligram per kilogram (mg/kg) as intravenous (IV) infusion on Day 1 of cycle 1. From cycle 2 onwards, subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.

Reporting group title	Part B: Decitabine

Reporting group description:

Subjects received decitabine on Days 1 to 5 of each 28-day cycle
until treatment failure, relapse from CR or CRi, unacceptable toxicity, or death.

Reporting group title	Part B: Decitabine + JNJ-56022473

Reporting group description:

Subjects received decitabine 20 milligram per meter square (mg/m^2) IV on Day 1 to Day 5 followed by 9 mg/kg JNJ-56022473 on Day 8 and Day 22 of a 28-day cycle until treatment failure, relapse from complete response/remission (CR) or complete response with incomplete recovery (CRi), unacceptable toxicity, or death.

Serious adverse events	Part A: Decitabine + JNJ-56022473	Part B: Decitabine	Part B: Decitabine + JNJ-56022473
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	120 / 165 (72.73%)	126 / 147 (85.71%)
number of deaths (all causes)	10	105	91
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Neoplasm			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Central Nervous System Leukaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chloroma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Adenoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional Cell Carcinoma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Adenocarcinoma Gastric			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemodynamic Instability			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter Site Inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General Physical Health Deterioration			
subjects affected / exposed	1 / 10 (10.00%)	6 / 165 (3.64%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 1	0 / 8	0 / 5
deaths causally related to treatment / all	1 / 1	3 / 3	0 / 3
Hyperthermia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Influenza Like Illness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	0 / 10 (0.00%)	9 / 165 (5.45%)	9 / 147 (6.12%)
occurrences causally related to treatment / all	0 / 0	2 / 11	0 / 11
deaths causally related to treatment / all	0 / 0	9 / 9	0 / 8
Pyrexia			

subjects affected / exposed	1 / 10 (10.00%)	9 / 165 (5.45%)	15 / 147 (10.20%)
occurrences causally related to treatment / all	0 / 1	2 / 12	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden Death			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	5 / 5	0 / 1
Condition Aggravated			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic Shock			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Serum Sickness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Pulmonary Oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Acute Respiratory Failure			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1
Bronchopneumopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 10 (20.00%)	1 / 165 (0.61%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infiltration			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Oropharyngeal Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			

subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Pulmonary Oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory Failure			
subjects affected / exposed	0 / 10 (0.00%)	3 / 165 (1.82%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 2
Respiratory Tract Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Wheezing			

subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (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
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-Reactive Protein Increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Fall			
subjects affected / exposed	0 / 10 (0.00%)	3 / 165 (1.82%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral Neck Fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip Fracture			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Humerus Fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Compression Fracture			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Transfusion Reaction			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion-Related Acute Lung Injury			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Traumatic Haematoma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina Pectoris			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	5 / 147 (3.40%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Arrest			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	5 / 147 (3.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 2
Cardiac Failure			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Cardiac Failure Acute			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Cardiogenic Shock			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary Failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1
Cardiovascular Insufficiency			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Myocardial Ischaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pericardial Effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular Tachycardia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage Intracranial			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Haemorrhagic Stroke			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Ischaemic Stroke			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadriparesis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Seizure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular Encephalopathy			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	6 / 165 (3.64%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 0	1 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated Intravascular Coagulation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Febrile Bone Marrow Aplasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
subjects affected / exposed	2 / 10 (20.00%)	36 / 165 (21.82%)	40 / 147 (27.21%)
occurrences causally related to treatment / all	0 / 2	26 / 49	0 / 67
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Splenomegaly			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	2 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Acute Abdomen			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Anal Ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Colitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis Ulcerative			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	3 / 165 (1.82%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular Perforation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum Intestinal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis Erosive			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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 Angiodysplasia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Polyp Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large Intestinal Obstruction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Mechanical Ileus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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	0 / 10 (0.00%)	1 / 165 (0.61%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Vomiting			
subjects affected / exposed	1 / 10 (10.00%)	1 / 165 (0.61%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (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
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cholangitis Acute			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis Acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash Vesicular			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	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 / 10 (0.00%)	0 / 165 (0.00%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Urinary			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
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 Retention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Bursitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondrocalcinosis Pyrophosphate			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Muscular Weakness			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in Extremity			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Actinomycotic Pulmonary Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alveolar Osteitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary Aspergillosis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter Site Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Device Related Infection			
subjects affected / exposed	2 / 10 (20.00%)	3 / 165 (1.82%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Sepsis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Enterobacter Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Escherichia Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Sepsis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Gastroenteritis Rotavirus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Viral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Infection Fungal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected Skin Ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious Colitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver Abscess			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection			
subjects affected / exposed	4 / 10 (40.00%)	5 / 165 (3.03%)	3 / 147 (2.04%)
occurrences causally related to treatment / all	0 / 5	2 / 6	0 / 3
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Meningitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Moraxella Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic Sepsis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Oral Candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae Virus Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Periorbital Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis Jirovecii Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	23 / 165 (13.94%)	24 / 147 (16.33%)
occurrences causally related to treatment / all	0 / 0	15 / 39	0 / 29
deaths causally related to treatment / all	0 / 0	9 / 9	0 / 5
Pneumonia Fungal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous Colitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Mycosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis Acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis Chronic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Rash Pustular			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	4 / 147 (2.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Rhinovirus Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 10 (20.00%)	6 / 165 (3.64%)	14 / 147 (9.52%)
occurrences causally related to treatment / all	0 / 3	2 / 6	0 / 21
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 7
Septic Encephalopathy			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Septic Shock			
subjects affected / exposed	0 / 10 (0.00%)	2 / 165 (1.21%)	8 / 147 (5.44%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 10
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 5
Sinusitis Fungal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 165 (0.61%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic Abscess			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth Abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth Infection			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	4 / 165 (2.42%)	6 / 147 (4.08%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (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

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

Non-serious adverse events	Part A: Decitabine + JNJ-56022473	Part B: Decitabine	Part B: Decitabine + JNJ-56022473
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	157 / 165 (95.15%)	146 / 147 (99.32%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	13 / 165 (7.88%)	24 / 147 (16.33%)
occurrences (all)	0	17	33
Hypotension			
subjects affected / exposed	1 / 10 (10.00%)	17 / 165 (10.30%)	22 / 147 (14.97%)
occurrences (all)	1	17	29
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 10 (20.00%)	25 / 165 (15.15%)	26 / 147 (17.69%)
occurrences (all)	5	45	44
Chills			
subjects affected / exposed	3 / 10 (30.00%)	7 / 165 (4.24%)	30 / 147 (20.41%)
occurrences (all)	3	8	44
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	31 / 165 (18.79%)	31 / 147 (21.09%)
occurrences (all)	3	37	41
Oedema Peripheral			

subjects affected / exposed	5 / 10 (50.00%)	25 / 165 (15.15%)	46 / 147 (31.29%)
occurrences (all)	9	44	70
Pain			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	8 / 147 (5.44%)
occurrences (all)	0	8	8
Pyrexia			
subjects affected / exposed	6 / 10 (60.00%)	46 / 165 (27.88%)	51 / 147 (34.69%)
occurrences (all)	11	91	79
Gait Disturbance			
subjects affected / exposed	2 / 10 (20.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences (all)	2	0	1
General Physical Health Deterioration			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	1 / 147 (0.68%)
occurrences (all)	1	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 10 (10.00%)	15 / 165 (9.09%)	16 / 147 (10.88%)
occurrences (all)	1	23	22
Dyspnoea			
subjects affected / exposed	3 / 10 (30.00%)	23 / 165 (13.94%)	22 / 147 (14.97%)
occurrences (all)	5	25	27
Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	13 / 165 (7.88%)	20 / 147 (13.61%)
occurrences (all)	1	17	24
Hypoxia			
subjects affected / exposed	1 / 10 (10.00%)	7 / 165 (4.24%)	8 / 147 (5.44%)
occurrences (all)	1	8	15
Oropharyngeal Pain			
subjects affected / exposed	0 / 10 (0.00%)	7 / 165 (4.24%)	9 / 147 (6.12%)
occurrences (all)	0	9	11
Pleural Effusion			
subjects affected / exposed	1 / 10 (10.00%)	10 / 165 (6.06%)	4 / 147 (2.72%)
occurrences (all)	1	13	4
Bronchospasm			

subjects affected / exposed	3 / 10 (30.00%)	1 / 165 (0.61%)	6 / 147 (4.08%)
occurrences (all)	3	2	7
Pharyngeal Oedema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 10 (20.00%)	13 / 165 (7.88%)	16 / 147 (10.88%)
occurrences (all)	2	16	21
Adjustment Disorder with Depressed Mood			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	1 / 10 (10.00%)	3 / 165 (1.82%)	4 / 147 (2.72%)
occurrences (all)	1	3	6
Depressed Mood			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Hallucination			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	1 / 147 (0.68%)
occurrences (all)	1	2	1
Nervousness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	9 / 147 (6.12%)
occurrences (all)	0	5	12
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	8 / 147 (5.44%)
occurrences (all)	0	6	10
Blood Creatinine Increased			
subjects affected / exposed	0 / 10 (0.00%)	4 / 165 (2.42%)	8 / 147 (5.44%)
occurrences (all)	0	4	12
Gamma-Glutamyltransferase Increased			

subjects affected / exposed	1 / 10 (10.00%)	1 / 165 (0.61%)	8 / 147 (5.44%)
occurrences (all)	1	1	11
Weight Decreased			
subjects affected / exposed	0 / 10 (0.00%)	10 / 165 (6.06%)	16 / 147 (10.88%)
occurrences (all)	0	12	22
Bacterial Test Positive			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	1 / 147 (0.68%)
occurrences (all)	2	0	1
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
International Normalised Ratio Increased			
subjects affected / exposed	1 / 10 (10.00%)	3 / 165 (1.82%)	4 / 147 (2.72%)
occurrences (all)	1	3	5
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	4 / 147 (2.72%)
occurrences (all)	1	0	4
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	8 / 147 (5.44%)
occurrences (all)	0	5	9
Fall			
subjects affected / exposed	0 / 10 (0.00%)	9 / 165 (5.45%)	13 / 147 (8.84%)
occurrences (all)	0	11	19
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	8 / 165 (4.85%)	13 / 147 (8.84%)
occurrences (all)	0	8	17
Tachycardia			
subjects affected / exposed	1 / 10 (10.00%)	6 / 165 (3.64%)	14 / 147 (9.52%)
occurrences (all)	2	7	15
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	9 / 165 (5.45%)	14 / 147 (9.52%)
occurrences (all)	1	10	17
Headache			

subjects affected / exposed	1 / 10 (10.00%)	15 / 165 (9.09%)	16 / 147 (10.88%)
occurrences (all)	1	20	17
Syncope			
subjects affected / exposed	2 / 10 (20.00%)	5 / 165 (3.03%)	6 / 147 (4.08%)
occurrences (all)	2	6	9
Somnolence			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	2 / 147 (1.36%)
occurrences (all)	1	2	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 10 (70.00%)	80 / 165 (48.48%)	77 / 147 (52.38%)
occurrences (all)	27	286	260
Febrile Neutropenia			
subjects affected / exposed	4 / 10 (40.00%)	22 / 165 (13.33%)	25 / 147 (17.01%)
occurrences (all)	7	32	34
Leukocytosis			
subjects affected / exposed	0 / 10 (0.00%)	9 / 165 (5.45%)	1 / 147 (0.68%)
occurrences (all)	0	10	1
Leukopenia			
subjects affected / exposed	1 / 10 (10.00%)	15 / 165 (9.09%)	12 / 147 (8.16%)
occurrences (all)	1	75	38
Neutropenia			
subjects affected / exposed	1 / 10 (10.00%)	61 / 165 (36.97%)	64 / 147 (43.54%)
occurrences (all)	11	196	201
Thrombocytopenia			
subjects affected / exposed	3 / 10 (30.00%)	86 / 165 (52.12%)	81 / 147 (55.10%)
occurrences (all)	7	341	252
Splenomegaly			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	2 / 147 (1.36%)
occurrences (all)	1	2	2
Ear and labyrinth disorders			
Tympanic Membrane Disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Uveitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 10 (10.00%)	12 / 165 (7.27%)	19 / 147 (12.93%)
occurrences (all)	1	14	28
Abdominal Pain Upper			
subjects affected / exposed	2 / 10 (20.00%)	6 / 165 (3.64%)	9 / 147 (6.12%)
occurrences (all)	3	6	12
Anal Incontinence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 165 (0.00%)	10 / 147 (6.80%)
occurrences (all)	0	0	11
Constipation			
subjects affected / exposed	3 / 10 (30.00%)	51 / 165 (30.91%)	47 / 147 (31.97%)
occurrences (all)	4	71	69
Diarrhoea			
subjects affected / exposed	4 / 10 (40.00%)	41 / 165 (24.85%)	50 / 147 (34.01%)
occurrences (all)	5	68	75
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)	5 / 165 (3.03%)	10 / 147 (6.80%)
occurrences (all)	1	5	12
Gingival Bleeding			
subjects affected / exposed	0 / 10 (0.00%)	10 / 165 (6.06%)	2 / 147 (1.36%)
occurrences (all)	0	11	2
Haemorrhoids			
subjects affected / exposed	1 / 10 (10.00%)	8 / 165 (4.85%)	21 / 147 (14.29%)
occurrences (all)	1	8	22
Nausea			
subjects affected / exposed	5 / 10 (50.00%)	33 / 165 (20.00%)	36 / 147 (24.49%)
occurrences (all)	10	44	58
Stomatitis			
subjects affected / exposed	1 / 10 (10.00%)	16 / 165 (9.70%)	12 / 147 (8.16%)
occurrences (all)	1	17	17
Toothache			

subjects affected / exposed	0 / 10 (0.00%)	9 / 165 (5.45%)	4 / 147 (2.72%)
occurrences (all)	0	9	4
Vomiting			
subjects affected / exposed	5 / 10 (50.00%)	19 / 165 (11.52%)	26 / 147 (17.69%)
occurrences (all)	8	32	42
Abdominal Discomfort			
subjects affected / exposed	1 / 10 (10.00%)	1 / 165 (0.61%)	6 / 147 (4.08%)
occurrences (all)	1	1	7
Parotid Gland Enlargement			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 10 (20.00%)	7 / 165 (4.24%)	3 / 147 (2.04%)
occurrences (all)	2	12	4
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	4 / 165 (2.42%)	9 / 147 (6.12%)
occurrences (all)	0	5	11
Petechiae			
subjects affected / exposed	1 / 10 (10.00%)	10 / 165 (6.06%)	11 / 147 (7.48%)
occurrences (all)	1	11	12
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	12 / 165 (7.27%)	11 / 147 (7.48%)
occurrences (all)	1	12	15
Rash			
subjects affected / exposed	1 / 10 (10.00%)	11 / 165 (6.67%)	13 / 147 (8.84%)
occurrences (all)	1	11	16
Hyperhidrosis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	7 / 147 (4.76%)
occurrences (all)	1	2	7
Dry Skin			

subjects affected / exposed	1 / 10 (10.00%)	3 / 165 (1.82%)	2 / 147 (1.36%)
occurrences (all)	1	3	2
Hidradenitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Purpura			
subjects affected / exposed	1 / 10 (10.00%)	1 / 165 (0.61%)	0 / 147 (0.00%)
occurrences (all)	1	1	0
Skin Ulcer			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	3 / 147 (2.04%)
occurrences (all)	1	3	4
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 10 (0.00%)	7 / 165 (4.24%)	11 / 147 (7.48%)
occurrences (all)	0	7	15
Urinary Incontinence			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	10 / 147 (6.80%)
occurrences (all)	0	6	11
Renal Impairment			
subjects affected / exposed	1 / 10 (10.00%)	3 / 165 (1.82%)	5 / 147 (3.40%)
occurrences (all)	1	4	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	15 / 165 (9.09%)	12 / 147 (8.16%)
occurrences (all)	1	16	16
Back Pain			
subjects affected / exposed	0 / 10 (0.00%)	18 / 165 (10.91%)	19 / 147 (12.93%)
occurrences (all)	0	19	26
Pain in Extremity			
subjects affected / exposed	0 / 10 (0.00%)	12 / 165 (7.27%)	15 / 147 (10.20%)
occurrences (all)	0	18	22
Muscle Spasms			
subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	2 / 147 (1.36%)
occurrences (all)	1	4	2
Muscular Weakness			

subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	2 / 147 (1.36%)
occurrences (all)	1	4	3
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	1 / 147 (0.68%)
occurrences (all)	1	4	1
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	3 / 165 (1.82%)	4 / 147 (2.72%)
occurrences (all)	1	3	4
Infections and infestations			
Oral Candidiasis			
subjects affected / exposed	2 / 10 (20.00%)	6 / 165 (3.64%)	9 / 147 (6.12%)
occurrences (all)	2	8	11
Oral Herpes			
subjects affected / exposed	3 / 10 (30.00%)	9 / 165 (5.45%)	11 / 147 (7.48%)
occurrences (all)	3	13	14
Pneumonia			
subjects affected / exposed	1 / 10 (10.00%)	19 / 165 (11.52%)	19 / 147 (12.93%)
occurrences (all)	1	24	25
Urinary Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	13 / 165 (7.88%)	13 / 147 (8.84%)
occurrences (all)	0	15	19
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)	5 / 165 (3.03%)	5 / 147 (3.40%)
occurrences (all)	1	5	9
Lung Infection			
subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	2 / 147 (1.36%)
occurrences (all)	1	4	2
Lymph Gland Infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal Candidiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	2 / 147 (1.36%)
occurrences (all)	1	0	3
Respiratory Tract Infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	3 / 147 (2.04%)
occurrences (all)	1	0	3

Skin Infection			
subjects affected / exposed	1 / 10 (10.00%)	3 / 165 (1.82%)	2 / 147 (1.36%)
occurrences (all)	1	4	5
Systemic Mycosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Tooth Abscess			
subjects affected / exposed	1 / 10 (10.00%)	0 / 165 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 10 (10.00%)	6 / 165 (3.64%)	2 / 147 (1.36%)
occurrences (all)	1	6	2
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	4 / 10 (40.00%)	31 / 165 (18.79%)	25 / 147 (17.01%)
occurrences (all)	4	38	37
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	4 / 165 (2.42%)	17 / 147 (11.56%)
occurrences (all)	0	4	25
Hyperuricaemia			
subjects affected / exposed	0 / 10 (0.00%)	8 / 165 (4.85%)	9 / 147 (6.12%)
occurrences (all)	0	11	12
Hypoalbuminaemia			
subjects affected / exposed	0 / 10 (0.00%)	5 / 165 (3.03%)	13 / 147 (8.84%)
occurrences (all)	0	7	15
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)	9 / 165 (5.45%)	14 / 147 (9.52%)
occurrences (all)	1	16	16
Hypokalaemia			
subjects affected / exposed	3 / 10 (30.00%)	41 / 165 (24.85%)	53 / 147 (36.05%)
occurrences (all)	5	64	99
Hypomagnesaemia			
subjects affected / exposed	2 / 10 (20.00%)	12 / 165 (7.27%)	20 / 147 (13.61%)
occurrences (all)	4	20	25
Hypophosphataemia			

subjects affected / exposed	1 / 10 (10.00%)	5 / 165 (3.03%)	9 / 147 (6.12%)
occurrences (all)	2	6	9
Fluid Overload			
subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	6 / 147 (4.08%)
occurrences (all)	1	5	6
Fluid Retention			
subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	1 / 147 (0.68%)
occurrences (all)	2	6	2
Hyperkalaemia			
subjects affected / exposed	1 / 10 (10.00%)	4 / 165 (2.42%)	5 / 147 (3.40%)
occurrences (all)	1	5	9
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 165 (1.21%)	2 / 147 (1.36%)
occurrences (all)	1	2	2
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)	7 / 165 (4.24%)	4 / 147 (2.72%)
occurrences (all)	1	8	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 January 2016	The overall reason for the amendment is that the study was originally designed as a Phase 2 study with a total of 120 subjects and a primary endpoint of event-free survival (EFS). An interim analysis with 45 EFS events was planned in the original study to determine if the study would be continued toward the end with 120 subjects. This amendment changes the primary endpoint of the study to 2 primary endpoints of complete response (CR) rate and overall survival (OS) and up to 400 subjects enrolled.
28 June 2016	This amendment was prepared in response to health authority review and clarifies inclusion criteria and the recommended dose of preinfusion medications prior to JNJ-56022473 administration
29 March 2017	The main reason of this amendment was to specify new guidance for patient monitoring and availability of resuscitation equipment during talacotuzumab infusion.
26 April 2017	The main reason of this amendment was to specify enhanced precautionary measures to mitigate infusion-related reactions for subjects receiving talacotuzumab infusion.
02 August 2017	The amendment was based on on Independent Data Monitoring Committee (IDMC) recommendation after results from the second interim analysis (final analysis for response endpoints and first analysis for overall survival [OS]) were reviewed. The IDMC recommended to close study enrollment and stop talacotuzumab treatment due to lack of efficacy in the talacotuzumab arm. Subjects in the combination arm should stop treatment of with talacotuzumab and can continue to receive DACOGEN only, in accordance with Principal Investigator decision and subject agreement.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported