Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Phase 1b/2 Study of LY2228820, a p38MAPK Inhibitor, plus Gemcitabine and Carboplatin versus Gemcitabine and Carboplatin for Women with Platinum-Sensitive Ovarian Cancer

Summary

EudraCT number	2011-005197-40
Trial protocol	DE BE
Global end of trial date	11 May 2018

Results information

Result version number	v1 (current)
This version publication date	24 May 2019
First version publication date	24 May 2019

Trial information

Trial identification

Sponsor protocol code	I1D-MC-JIAE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01663857
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias: 12517

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46825
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	11 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase 1b - to determine the recommended Phase 2 dose of LY2228820 that can be safely administered with gemcitabine and carboplatin
Phase 2 - to compare the progression-free survival in patients treated with LY2228820 plus gemcitabine and carboplatin versus placebo plus gemcitabine and carboplatin

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	United States: 62
Worldwide total number of subjects	118
EEA total number of subjects	46

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)	67
From 65 to 84 years	51
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants in Phase 1b are considered to have completed the study if they experience a dose-limiting toxicity or completed the Pharmacokinetic (PK) sampling set. Participants in Phase 2 are considered to have completed if they die due to any cause or who are alive and on study at conclusion, but are off treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1b: Cohort 1: LY2228820 + Gemcitabine + Carboplatin

Arm description:

Cohort 1: LY2228820 200 milligrams (mg) administered orally every 12 hours (hr) on Days 1-10 of a 21-day cycle (Cycles 1-6).

Gemcitabine 1000 milligrams per square meter (mg/m^2) administered intravenously (IV) over 30 minutes (min) on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin area under the concentration curve (AUC) 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Cohort 1: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day cycle (Cycles 7+).

Arm type	Experimental
Investigational medicinal product name	LY2228820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

LY2228820 200 milligrams (mg) administered orally every 12 hours on days 1-10 of Cycles 1-6.

LY2228820 300 mg administered orally every 12 hours on days 1-14 of Cycles 7+

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	LY188011
Other name	Gemzar
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6)

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

Dosage and administration details:

Carboplatin AUC 4 (max dose 600 mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6)

Arm title	Phase 1b : Cohort 2: LY2228820 + Gemcitabine + Carboplatin

Arm description:

Cohort 2: LY2228820 300 mg administered orally every 12 hours on Days 1-10 of 21-day Cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Cohort 2: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28-day cycle (Cycles 7+).

Arm type	Experimental
Investigational medicinal product name	LY2228820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

LY2228820 200 mg administered orally every 12 hours on days 1-10 of 21-day cycle (Cycles 1-6).

LY2228820 300 mg administered orally every 12 hours on days 1-14 of a 28-day cycle (Cycles 7+).

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	LY188011
Other name	Gemzar
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes (min) on Days 3 and 10 of a 21-day cycle (Cycles 1-6)

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

Dosage and administration details:

Carboplatin AUC 4 (max dose 600 mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6)

Arm title	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin

Arm description:

Arm A: LY2228820 200 mg orally every 12 hours on Days 1-10 of 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Arm A: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day-cycle (Cycles 7+).

Arm type	Experimental

Investigational medicinal product name	LY2228820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

LY2228820 200 mg administered orally every 12 hours on days 1-10 of 21-day cycle (Cycles 1-6).

LY2228820 300 mg administered orally every 12 hours on days 1-14 of a 28-day cycle (Cycles 7+).

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	LY188011
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6)

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

Dosage and administration details:

Carboplatin AUC 4 (max dose 600 mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6)

Arm title	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin

Arm description:

Arm B: Placebo orally every 12 hours on Days 1-10 of 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Arm B: Placebo orally every 12 hr. on Days 1-14 of a 28-day cycle (Cycles 7+)

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

Dosage and administration details:

Placebo administered orally every 12 hours on days 1-10 of 21-day cycle (Cycles 1-6).

Placebo administered orally every 12 hours on days 1-14 of a 28-day cycle (Cycles 7+).

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	LY188011
Other name	Gemzar
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6)

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin AUC 4 (max dose 600 mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6)

Number of subjects in period 1	Phase 1b: Cohort 1: LY2228820 + Gemcitabine + Carboplatin	Phase 1b : Cohort 2: LY2228820 + Gemcitabine + Carboplatin	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin
Started	6	2	58
Recieved at Least One Dose of Study Drug	6	2	58
Completed	6	1	48
Not completed	0	1	10
Consent withdrawn by subject	-	1	7
Lost to follow-up	-	-	3

Number of subjects in period 1	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin
Started	52
Recieved at Least One Dose of Study Drug	52
Completed	48
Not completed	4
Consent withdrawn by subject	3
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Phase 1b: Cohort 1: LY2228820 + Gemcitabine + Carboplatin

Reporting group description:

Cohort 1: LY2228820 200 milligrams (mg) administered orally every 12 hours (hr) on Days 1-10 of a 21-day cycle (Cycles 1-6).

Gemcitabine 1000 milligrams per square meter (mg/m^2) administered intravenously (IV) over 30 minutes (min) on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin area under the concentration curve (AUC) 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Cohort 1: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day cycle (Cycles 7+).

Reporting group title	Phase 1b : Cohort 2: LY2228820 + Gemcitabine + Carboplatin

Reporting group description:

Cohort 2: LY2228820 300 mg administered orally every 12 hours on Days 1-10 of 21-day Cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Cohort 2: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28-day cycle (Cycles 7+).

Reporting group title	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin

Reporting group description:

Arm A: LY2228820 200 mg orally every 12 hours on Days 1-10 of 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Arm A: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day-cycle (Cycles 7+).

Reporting group title	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin

Reporting group description:

Arm B: Placebo orally every 12 hours on Days 1-10 of 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Arm B: Placebo orally every 12 hr. on Days 1-14 of a 28-day cycle (Cycles 7+)

Reporting group values	Phase 1b: Cohort 1: LY2228820 + Gemcitabine + Carboplatin	Phase 1b : Cohort 2: LY2228820 + Gemcitabine + Carboplatin	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin
Number of subjects	6	2	58
Age categorical Units: Subjects			
18-64 years	4	1	32
65-84 years	2	1	26

Gender categorical Units: Subjects			
Female	6	2	58
Male	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	6	1	57
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Belgium	0	0	11
United States	5	2	30
Australia	0	0	4
Germany	1	0	13
Maintenance Therapy as a Part of or After a First Line Platinum Regimen			
Measure Analysis Population Description: Maintenance therapy as part of or after first line platinum regimen data was used as a cofactor in the analysis of Progression Free Survival (PFS). Zero participants analyzed for Phase 1 portion of the study. Data was collected only from participants treated in the Phase 2 portion of the study.			
Units: Subjects			
Received Maintenance Therapy	0	0	7
Did Not Receive Maintenance Therapy	0	0	15
Data Missing or Not Collected	6	2	36

Reporting group values	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin	Total	
Number of subjects	52	118	
Age categorical Units: Subjects			
18-64 years	30	67	
65-84 years	22	51	
Gender categorical Units: Subjects			
Female	52	118	
Male	0	0	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	2	
White	49	113	
More than one race	0	0	
Unknown or Not Reported	1	1	

Region of Enrollment Units: Subjects			
Belgium	9	20	
United States	25	62	
Australia	6	10	
Germany	12	26	
Maintenance Therapy as a Part of or After a First Line Platinum Regimen			
Measure Analysis Population Description: Maintenance therapy as part of or after first line platinum regimen data was used as a cofactor in the analysis of Progression Free Survival (PFS). Zero participants analyzed for Phase 1 portion of the study. Data was collected only from participants treated in the Phase 2 portion of the study.			
Units: Subjects			
Received Maintenance Therapy	7	14	
Did Not Receive Maintenance Therapy	15	30	
Data Missing or Not Collected	30	74	

End points

End points reporting groups

Reporting group title	Phase 1b: Cohort 1: LY2228820 + Gemcitabine + Carboplatin

Reporting group description:

Cohort 1: LY2228820 200 milligrams (mg) administered orally every 12 hours (hr) on Days 1-10 of a 21-day cycle (Cycles 1-6).

Gemcitabine 1000 milligrams per square meter (mg/m^2) administered intravenously (IV) over 30 minutes (min) on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin area under the concentration curve (AUC) 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Cohort 1: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day cycle (Cycles 7+).

Reporting group title	Phase 1b : Cohort 2: LY2228820 + Gemcitabine + Carboplatin

Reporting group description:

Cohort 2: LY2228820 300 mg administered orally every 12 hours on Days 1-10 of 21-day Cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Cohort 2: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28-day cycle (Cycles 7+).

Reporting group title	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin

Reporting group description:

Arm A: LY2228820 200 mg orally every 12 hours on Days 1-10 of 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Arm A: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day-cycle (Cycles 7+).

Reporting group title	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin

Reporting group description:

Arm B: Placebo orally every 12 hours on Days 1-10 of 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m^2 administered intravenously (IV) over 30 minutes on Days 3 and 10 of a 21-day cycle (Cycles 1-6).

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3 of a 21-day cycle (Cycles 1-6).

Arm B: Placebo orally every 12 hr. on Days 1-14 of a 28-day cycle (Cycles 7+)

Subject analysis set title	Phase 1b
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Phase 1b: Cohort 1: LY2228820 +Gemcitabine + Carboplatin: Cohort 1: LY2228820 200 milligrams (mg) administered orally every 12 hours (hr) on Days 1-10 of a 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg per square meter (m2) administered intravenously (IV) over 30 minutes (min) on Days 3 and 10.

Carboplatin area under the concentration curve administered intravenously (IV) over 30 minutes (AUC) 4 (maximum dose 600mg) IV over 30 min. on Day 3.

Phase 1b: Cohort 2: LY2228820 + Gemcitabine + Carboplatin: Cohort 2: LY2228820 300 milligrams (mg) administered orally every 12 hr. on Days 1-10 of a 21-day cycle (Cycles 1-6).

Gemcitabine 1000 mg/m2 administered intravenously (IV) over 30 min on Days 3 and 10.

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 min. on Day 3.

Cohort 2: LY2228820 300 mg orally every 12 hr. on Days 1-14

Subject analysis set title	LY2228820 200 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Phase 1b (Cohort 1) and Phase 2 Arm A: LY2228820 200 mg administered orally every 12 hours on Days 1-10, Cycles 1-6 of a 21 day cycle.

Subject analysis set title	LY2228820 300 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Phase 1b (Cohort 2) and Phase 2 (Arm A) in the maintenance portion with LY2228820 300 mg administered orally every 12 hours on Days 1-14 Cycle 7+ on a 28 day cycle.

Subject analysis set title	Arm A: LY2228820 + Gemcitabine + Carboplatin
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Arm A: LY2228820 200 mg orally every 12 hr. on Days 1-10 (Cycles 1-6).

Gemcitabine 1000 mg/m2 IV over 30 minutes on Days 3 and 10.

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3.

Arm A: LY2228820 300 mg orally every 12 hr. on Days 1-14 of a 28 day cycle (Cycles 7+).

Subject analysis set title	Arm B Placebo + Gemcitabine +Carboplatin
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Arm B: Placebo orally every 12 hrs. on Days 1-10 (Cycles 1-6).

Gemcitabine 1000 mg/m2 IV over 30 minutes on Days 3 and 10.

Carboplatin AUC 4 (maximum dose 600mg) IV over 30 minutes on Day 3.

Arm B: Placebo orally every 12 hr. on Days 1-14 of a 28 day cycle (Cycles 7+).

Primary: Phase 1b: Recommended Phase 2 Dose of LY2228820 in Combination with Gemcitabine and Carboplatin (Maximum Tolerated Dose [MTD])

End point title	Phase 1b: Recommended Phase 2 Dose of LY2228820 in Combination with Gemcitabine and Carboplatin (Maximum Tolerated Dose [MTD])[1]

End point description:

Recommended Phase 2 dose of LY2228820 that could be safely administered in combination with gemcitabine and carboplatin based on defined dose limiting toxicities (DLT) assessment and MTD definition. The MTD is defined as the highest dose level at which no more than 33% of patients experience a DLT during Cycle 1 that does not exceed the single-agent MTD for LY2228820 (300 mg Q12H).

End point type	Primary

End point timeframe:

Cycle 1 (21 Days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not performed for Recommended Phase 2 Dose for this primary endpoint as there were no comparison groups.

End point values	Phase 1b			
Subject group type	Subject analysis set			
Number of subjects analysed	8[2]			
Units: milligrams (mg)				
number (not applicable)	200			

Notes:

[2] - All participants who received at least one dose of study drug in Phase 1b.

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Progression-free Survival (PFS) in Participants Treated With LY2228820 Plus Gemcitabine and Carboplatin Versus Placebo Plus Gemcitabine and Carboplatin

End point title	Phase 2: Progression-free Survival (PFS) in Participants Treated With LY2228820 Plus Gemcitabine and Carboplatin Versus Placebo Plus Gemcitabine and Carboplatin[3]

End point description:

PFS was defined as time from date of randomization to the date of investigator-determined objective progression as defined by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 or death due to any cause, whichever occurred first. Progressive disease (PD) is defined as at least a 20% increase in the sum of the largest diameter (LD) of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.

End point type	Primary

End point timeframe:

Baseline to Date of Disease Progression or Death from any cause (up to 3 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: Phase 1b was conducted to determine recommended Phase 2 dose, PFS was assessed on participants in Phase 2 only.

End point values	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[4]	52[5]		
Units: Months				
median (confidence interval 90%)	10.25 (7.85 to 10.87)	8.44 (7.56 to 9.33)		

Notes:

[4] - All participants in Phase 2 who received at least one dose of study drug.

[5] - All participants in Phase 2 who received at least one dose of study drug.

Statistical analyses

Statistical analysis title	Phase 2 Progression-free Survival
Comparison groups	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin v Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	Logrank

Secondary: Phase 2: Percentage of Participants Who Achieve Complete Response or Partial Response (Overall Response Rate)

End point title	Phase 2: Percentage of Participants Who Achieve Complete Response or Partial Response (Overall Response Rate)[6]

End point description:

Overall Response Rate was estimated as the percentage of participants with best response of Complete Response (CR) or Partial Response (PR), based on RECIST version 1.1 divided by the total number of randomized participants. CR is defined as disappearance of all target lesions. PR is defined as at least 30% disease in the sum of the largest diameter (LD) of target lesions, taking as reference the baseline sum LD.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression (up to 3 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: Phase 1b was conducted to determine recommended Phase 2 dose, Overall Response Rate was assessed on participants in Phase 2 only.

End point values	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[7]	52[8]		
Units: Percentage of Participants				
number (not applicable)	46.6	46.2		

Notes:

[7] - All participants who received at least one dose of study drug in Phase 2.

[8] - All participants who received at least one dose of study drug in Phase 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival

End point title	Phase 2: Overall Survival[9]

End point description:

Data presented are the median overall survival in months for participants in the Phase 2 treatment arms.

End point type	Secondary

End point timeframe:

Baseline to Date of Death from any cause (up to 5 years)

Notes:

[9] - 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: Phase 1b was conducted to determine recommended Phase 2 dose, overall survival data was collected for participants in Phase 2 only.

End point values	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[10]	52[11]		
Units: Months				
median (confidence interval 90%)	29.17 (23.26 to 52.40)	25.10 (21.95 to 33.68)		

Notes:

[10] - All participants who received at least one dose of study drug in Phase 2.

[11] - All participants who received at least one dose of study drug in Phase 2.

Statistical analyses

Statistical analysis title	Phase 2: Overall Survival
Comparison groups	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin v Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4686
Method	Logrank

Secondary: Phase 1b and 2: Pharmacokinetics (PK): Area Under the Concentration Versus Time Curve From Time Zero to 8 Hours [AUC(0-8)] of LY2228820

End point title	Phase 1b and 2: Pharmacokinetics (PK): Area Under the Concentration Versus Time Curve From Time Zero to 8 Hours [AUC(0-8)] of LY2228820

End point description:

PK parameters after administration of LY2228820 for both Phase 1b and Phase 2.

Analysis Population Description: All participants in Phase 1b and Phase 2 who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Phase 1b:Cycle(C)1 Day(D)1:Predose(PRD),0.5,1,2,4,6,8 hours(hr)postdose(PD); C1D10:PRD,0.5,1,2,8hrPD; C2D10:PRD,0.5,1,2,4,6,8,12hrPD; C7D3:PRD,0.5,1,2,4,6hrPD; Phase 2: C1D3:PRD,0.5,1,2,4,6,8hrPD; C1D10:PRD,0.5,1,2,4,6,8hrPD; C7D3:PRD,0.5,1,2,4,6,8hrPD

End point values	LY2228820 200 mg	LY2228820 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13[12]	10[13]		
Units: nanograms*hr per milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=6, n=2)	3470 (± 91)	3560 (± 1)		
Cycle 1 Day 3 (n=7, n=0)	3170 (± 22)	0 (± 0)		
Cycle 1 Day 10 (n=11, n=1)	4270 (± 62)	9350 (± 0)		

Cycle 2 Day 10 (n=5, n=1)	3270 (± 38)	3490 (± 0)		
Cycle 7 Day 3 (n=0, n=10)	0 (± 0)	7230 (± 72)		

Notes:

[12] - Zero participants analyzed for LY2228820 200 mg Cycle 7 Day 3, no evaluable PK data.

[13] - Zero participants analyzed for LY2228820 300 mg Cycle 1 Day 3, no evaluable PK data.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Change From Baseline in Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O) Score

End point title	Phase 2: Change From Baseline in Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O) Score[14]

End point description:

The Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O) instrument measures health related quality of life (HRQoL) in participants with ovarian cancer. The instrument is organized into sections of physical, social/family, emotional, functional well-being and ovarian subscales with a 5-point rating scale in which 0 = "not at all" and 4 = "very much." Data presented here are change from baseline at follow-up in the FACT-O Total Score. The total score is the sum of Physical Well Being (PWB) + Social Well-being (SWB) + Emotional Well Being (EWB) + Family Well-being (FWB) + Ovarian Cancer Subscale (OCS). The FACT-O Total score range 0 - 152 with higher scores indicating better quality of life.

Analysis Population Description: All participants in Phase 2 who received at least one dose of study drug and had at least one post baseline assessment.

End point type	Secondary

End point timeframe:

Baseline, Study Completion (up to 3 years)

Notes:

[14] - 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: Phase 1b was conducted to determine recommended Phase 2 dose, Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O) Score was assessed on Phase 2 participants only.

End point values	Phase 2: Arm A: LY2228820 + Gemcitabine + Carboplatin	Phase 2: Arm B: Placebo + Gemcitabine + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	52		
Units: Units on a Scale				
arithmetic mean (standard deviation)	-0.6 (± 21.14)	-8.9 (± 19.92)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 4.5 years	
Adverse event reporting additional description: I1D-MC-JIAE	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Phase 1b: LY2228820-200mg+Gemcitabine+Carboplatin
Reporting group description: -	
Reporting group title	Phase 1b: LY2228820-300mg+Gemcitabine+Carboplatin
Reporting group description: -	
Reporting group title	Phase 2: LY2228820-200mg+Gemcitabine+Carboplatin
Reporting group description: -	
Reporting group title	Phase 2: Placebo+Gemcitabine+Carboplatin
Reporting group description: -	

Serious adverse events	Phase 1b: LY2228820-200mg+Gemcitabine+Carboplatin	Phase 1b: LY2228820-300mg+Gemcitabine+Carboplatin	Phase 2: LY2228820-200mg+Gemcitabine+Carboplatin
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	1 / 2 (50.00%)	26 / 58 (44.83%)
number of deaths (all causes)	3	1	30
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
general physical health deterioration			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
malaise			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			

alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
aspartate aminotransferase increased			

alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nuclear magnetic resonance imaging abdominal abnormal			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
platelet count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
cervical vertebral fracture			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fall			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infusion related reaction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thermal burn			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urostomy complication			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
headache			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
presyncope			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
febrile neutropenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutropenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal pain			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal pain upper			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ascites			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
constipation			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

small intestinal obstruction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subileus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
drug reaction with eosinophilia and systemic symptoms			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	0 / 58 (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
rash maculo-papular			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

acute kidney injury			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
flank pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
joint effusion			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
abscess			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
appendicitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
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			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clostridium difficile infection			

alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pelvic infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyelonephritis acute			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureteritis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hypokalaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypophosphataemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2: Placebo+Gemcitabine+Carboplatin		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 52 (23.08%)		

number of deaths (all causes)	31		
number of deaths resulting from adverse events	1		
General disorders and administration site conditions			
general physical health deterioration			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
malaise			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pyrexia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pleural effusion			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pneumonitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
nuclear magnetic resonance imaging abdominal abnormal			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
platelet count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
cervical vertebral fracture			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
fall			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
infusion related reaction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
thermal burn			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
urostomy complication			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
headache			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
presyncope				
alternative dictionary used: MedDRA 20.1				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
syncope				
alternative dictionary used: MedDRA 20.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
anaemia				
alternative dictionary used: MedDRA 20.1				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
febrile neutropenia				
alternative dictionary used: MedDRA 20.1				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
leukopenia				
alternative dictionary used: MedDRA 20.1				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
neutropenia				
alternative dictionary used: MedDRA 20.1				

subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
thrombocytopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
abdominal pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
abdominal pain upper			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ascites			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
constipation			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
diarrhoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ileus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
nausea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
small intestinal obstruction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
subileus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
vomiting			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
cholecystitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
drug reaction with eosinophilia and systemic symptoms			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
rash maculo-papular			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
flank pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
joint effusion			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
abscess			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
appendicitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
bacteraemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
clostridium difficile infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
erysipelas			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
gastroenteritis			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
lung infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pelvic infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pneumonia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
pyelonephritis acute			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
sepsis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ureteritis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

urinary tract infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
hypokalaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
hypophosphataemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1b: LY2228820-200mg+Gemcitabine+Carboplatin	Phase 1b: LY2228820-300mg+Gemcitabine+Carboplatin	Phase 2: LY2228820-200mg+Gemcitabine+Carboplatin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	2 / 2 (100.00%)	58 / 58 (100.00%)
Vascular disorders			
flushing			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
hypertension			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	3
General disorders and administration site conditions			

chills			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	1	0	1
fatigue			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 6 (83.33%)	0 / 2 (0.00%)	40 / 58 (68.97%)
occurrences (all)	11	0	50
oedema peripheral			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	7 / 58 (12.07%)
occurrences (all)	0	0	9
peripheral swelling			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
pyrexia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	8 / 58 (13.79%)
occurrences (all)	1	0	9
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	7
Social circumstances			
social problem			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	0 / 58 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
vaginal discharge			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0

vulvovaginal pruritus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	2
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	11 / 58 (18.97%)
occurrences (all)	0	1	11
dyspnoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	17 / 58 (29.31%)
occurrences (all)	0	0	20
dyspnoea exertional			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
epistaxis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	5 / 58 (8.62%)
occurrences (all)	0	2	6
hypoxia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
nasal congestion			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	7 / 58 (12.07%)
occurrences (all)	0	1	7
oropharyngeal pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	7 / 58 (12.07%)
occurrences (all)	2	0	7
paranasal sinus discomfort			
alternative dictionary used:			

MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
productive cough			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	1	0	1
rhinitis allergic			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	2
sleep apnoea syndrome			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
adjustment disorder with depressed mood			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
anxiety			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	4 / 58 (6.90%)
occurrences (all)	2	0	5
insomnia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	1 / 2 (50.00%)	3 / 58 (5.17%)
occurrences (all)	2	1	3
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	1 / 2 (50.00%)	25 / 58 (43.10%)
occurrences (all)	5	2	42
aspartate aminotransferase increased			

alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 6 (50.00%)	0 / 2 (0.00%)	17 / 58 (29.31%)
occurrences (all)	5	0	28
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	9 / 58 (15.52%)
occurrences (all)	2	0	12
blood creatinine increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	2
blood urea increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	0 / 58 (0.00%)
occurrences (all)	0	1	0
ejection fraction decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
haemoglobin decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	2
lymphocyte count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	3
neutrophil count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	26 / 58 (44.83%)
occurrences (all)	0	1	76
platelet count decreased			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	1 / 6 (16.67%)	1 / 2 (50.00%)	21 / 58 (36.21%)
occurrences (all)	6	2	53
weight decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	2
white blood cell count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 6 (50.00%)	0 / 2 (0.00%)	20 / 58 (34.48%)
occurrences (all)	12	0	47
Injury, poisoning and procedural complications			
infusion related reaction			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	7 / 58 (12.07%)
occurrences (all)	3	0	8
wrist fracture			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
palpitations			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	6 / 58 (10.34%)
occurrences (all)	0	0	6
sinus bradycardia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	12 / 58 (20.69%)
occurrences (all)	2	0	13
dysgeusia			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	5
headache			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 6 (50.00%)	0 / 2 (0.00%)	10 / 58 (17.24%)
occurrences (all)	4	0	10
paraesthesia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	3	0	6
syncope			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	2	0	1
tremor			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	6 / 58 (10.34%)
occurrences (all)	0	0	7
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 6 (83.33%)	1 / 2 (50.00%)	32 / 58 (55.17%)
occurrences (all)	8	4	91
increased tendency to bruise			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
leukocytosis			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	8
leukopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	3
neutropenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 6 (83.33%)	2 / 2 (100.00%)	26 / 58 (44.83%)
occurrences (all)	24	4	72
thrombocytopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 6 (66.67%)	0 / 2 (0.00%)	17 / 58 (29.31%)
occurrences (all)	9	0	40
Ear and labyrinth disorders			
tinnitus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	4 / 58 (6.90%)
occurrences (all)	0	0	4
vertigo			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	2	0	2
Eye disorders			
glaucoma			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
vision blurred			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
visual impairment			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
abdominal distension			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	6 / 58 (10.34%)
occurrences (all)	0	1	6
abdominal pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	12 / 58 (20.69%)
occurrences (all)	1	0	13
abdominal pain upper			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	5
anal incontinence			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
constipation			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	1 / 2 (50.00%)	23 / 58 (39.66%)
occurrences (all)	5	1	31
diarrhoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 6 (66.67%)	1 / 2 (50.00%)	23 / 58 (39.66%)
occurrences (all)	5	1	40
dry mouth			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	2
dyspepsia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	1	0	3
dysphagia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	2	0	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	3 / 58 (5.17%)
occurrences (all)	0	1	3
mouth ulceration			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	2
nausea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 6 (66.67%)	0 / 2 (0.00%)	31 / 58 (53.45%)
occurrences (all)	8	0	39
rectal haemorrhage			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
stomatitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	9 / 58 (15.52%)
occurrences (all)	2	0	10
vomiting			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 6 (50.00%)	0 / 2 (0.00%)	17 / 58 (29.31%)
occurrences (all)	3	0	23

Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	10 / 58 (17.24%)
occurrences (all)	0	1	10
dry skin			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
pruritus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	7 / 58 (12.07%)
occurrences (all)	0	0	10
pruritus generalised			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
rash			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	4 / 58 (6.90%)
occurrences (all)	0	0	5
Renal and urinary disorders			
dysuria			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	2
pollakiuria			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
urinary incontinence			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

arthralgia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	6 / 58 (10.34%)
occurrences (all)	0	0	6
back pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	7 / 58 (12.07%)
occurrences (all)	1	0	10
bone pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	5
flank pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	2
muscle spasms			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	4
myalgia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	5
neck pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	4 / 58 (6.90%)
occurrences (all)	0	0	4
osteoarthritis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
osteopenia			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
pain in extremity			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	4 / 58 (6.90%)
occurrences (all)	1	0	7
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	2
cystitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
fungal skin infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	2
pneumonia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
sinusitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 6 (50.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	4	0	1
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	5 / 58 (8.62%)
occurrences (all)	0	0	6
urinary tract infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	8 / 58 (13.79%)
occurrences (all)	1	0	14
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 6 (50.00%)	0 / 2 (0.00%)	14 / 58 (24.14%)
occurrences (all)	3	0	15
dehydration			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	1	0	1
hyperglycaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 6 (16.67%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	1	0	2
hyperkalaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	4
hyperuricaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	2 / 58 (3.45%)
occurrences (all)	0	1	2
hypocalcaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 2 (0.00%)	2 / 58 (3.45%)
occurrences (all)	0	0	4
hypokalaemia			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	2 / 6 (33.33%)	0 / 2 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	5
hypomagnesaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 6 (0.00%)	1 / 2 (50.00%)	7 / 58 (12.07%)
occurrences (all)	0	1	11

Non-serious adverse events	Phase 2: Placebo+Gemcitabine+Carboplatin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 52 (100.00%)		
Vascular disorders			
flushing			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	5		
hypertension			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
General disorders and administration site conditions			
chills			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	5		
fatigue			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	38 / 52 (73.08%)		
occurrences (all)	48		
oedema peripheral			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	8		
peripheral swelling			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
pyrexia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	7		
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Social circumstances			
social problem			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
vaginal discharge			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
vulvovaginal pruritus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	12		
dyspnoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	10		
dyspnoea exertional			

alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
epistaxis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
hypoxia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
nasal congestion			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	5		
oropharyngeal pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
paranasal sinus discomfort			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
productive cough			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
rhinitis allergic			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
sleep apnoea syndrome			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
adjustment disorder with depressed mood			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
anxiety			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
insomnia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	13 / 52 (25.00%)		
occurrences (all)	35		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	10 / 52 (19.23%)		
occurrences (all)	22		
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	7		
blood creatinine increased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
blood urea increased			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
ejection fraction decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
haemoglobin decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
lymphocyte count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	5		
neutrophil count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	29 / 52 (55.77%)		
occurrences (all)	92		
platelet count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	20 / 52 (38.46%)		
occurrences (all)	66		
weight decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	5		
white blood cell count decreased			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	19 / 52 (36.54%)		
occurrences (all)	55		
Injury, poisoning and procedural complications			
infusion related reaction			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	11		
wrist fracture			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Cardiac disorders			
palpitations			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	9		
sinus bradycardia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	9		
dysgeusia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
headache			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	20		
paraesthesia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
syncope			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
tremor			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	25 / 52 (48.08%)		
occurrences (all)	73		
increased tendency to bruise			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
leukocytosis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
leukopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
neutropenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	26 / 52 (50.00%)		
occurrences (all)	74		
thrombocytopenia			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	14 / 52 (26.92%)		
occurrences (all)	47		
Ear and labyrinth disorders			
tinnitus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
vertigo			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	4		
Eye disorders			
glaucoma			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
vision blurred			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
visual impairment			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	5		
abdominal distension			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	13		
abdominal pain			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	9		
abdominal pain upper			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	7		
anal incontinence			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
constipation			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	22 / 52 (42.31%)		
occurrences (all)	24		
diarrhoea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	14 / 52 (26.92%)		
occurrences (all)	18		
dry mouth			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
dyspepsia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
dysphagia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		

mouth ulceration			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
nausea			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	33 / 52 (63.46%)		
occurrences (all)	50		
rectal haemorrhage			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	5		
stomatitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	10 / 52 (19.23%)		
occurrences (all)	11		
vomiting			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	12		
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	10 / 52 (19.23%)		
occurrences (all)	10		
dry skin			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
pruritus			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	7		
pruritus generalised			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
rash			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	6		
Renal and urinary disorders			
dysuria			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
pollakiuria			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
urinary incontinence			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	7		
back pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	13		
bone pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	2		
flank pain			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
muscle spasms			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	6		
myalgia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	6		
neck pain			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
osteoarthritis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
osteopenia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
pain in extremity			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
cystitis			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
fungal skin infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
nasopharyngitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
pneumonia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
sinusitis			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
urinary tract infection			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	10		
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	13		
dehydration			
alternative dictionary used: MedDRA 20.1			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
hyperglycaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
hyperkalaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
hyperuricaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
hypocalcaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
hypokalaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	7		
hypomagnesaemia			
alternative dictionary used: MedDRA 20.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2014	Modification of dose limiting toxicity (DLT) criteria to account for expected toxicities with the combination of gemcitabine and carboplatin.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 September 2013	Enrollment was placed on hold to amend protocol to modify the dose limiting toxicity (DLT) criteria to account for expected toxicities from gemcitabine and carboplatin and to assess 300 mg LY2228820 in combination with gemcitabine and carboplatin.	-

Notes:

Limitations and caveats

None reported