Clinical trial results:
A Phase 1/Randomized Phase 2 Study to Evaluate LY2603618 in Combination With Gemcitabine in Patients With Pancreatic Cancer

Summary

EudraCT number	2008-006209-17
Trial protocol	DE SK PL IT
Global end of trial date	09 December 2013

Results information

Result version number	v1 (current)
This version publication date	06 March 2018
First version publication date	06 March 2018

Trial information

Trial identification

Sponsor protocol code	I2I-MC-JMMC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00839332
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 12096

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
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	09 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the Phase 1 portion of this study was to determine the dose of LY2603618 that can be safely administered 24 hours after gemcitabine treatment. This dose was then used for the Phase 2 portion of the study. The Phase 2 portion of the study evaluated whether LY2603618, when administered 24 hours after gemcitabine therapy, was an effective treatment for participants with pancreatic cancer

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	26 February 2009
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	United States: 73
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 2
Worldwide total number of subjects	149
EEA total number of subjects	76

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)	80
From 65 to 84 years	68
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No Text Entered

Period 1

Period 1 title	Phase 1/2 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: LY2603618 + Gemcitabine

Arm description:

All participants in Phase 1 received LY2603618 in combination with gemcitabine.

LY2603618: 70 to 250 milligrams/meter squared (mg/m^2) LY2603618 as a 1-hour continuous intravenous (IV) infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received LY2603618 as part of the dose escalation cohort of Phase 1 (dose of 70, 105, 150, 200, or 250 mg/m^2) or as part of the expansion cohort of Phase 1 (flat dose of 200 or 230 mg). The flat dose cohorts were conducted in parallel.

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Arm type	Experimental
Investigational medicinal product name	LY2603618
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

75 to 250 milligrams/meter squared (mg/m^2) LY2603618 as a 1-hour continuous intravenous (IV) infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression (DP). Participants received LY2603618 as part of the dose escalation cohort (dose of 70, 105, 150, 200, or 250 mg/m^2) or the expansion cohort (flat dose of 200 mg or 230 mg).

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

Dosage and administration details:

1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until DP. Participants received gemcitabine 24 hours prior to LY2603618 administration

Arm title	Phase 2: LY2603618 + Gemcitabine

Arm description:

LY2603618: 230 mg flat dose LY2603618 as a 1-hour continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Gemcitabine: Participants were administered 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Arm type	Experimental
Investigational medicinal product name	LY2603618
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

230 mg flat dose LY2603618 as a 1-hour continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

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

Dosage and administration details:

1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Arm title	Phase 2: Gemcitabine

Arm description:

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Arm type	Active comparator
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Number of subjects in period 1	Phase 1: LY2603618 + Gemcitabine	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine
Started	50	65	34
Received at least 1 dose of study drug	50	65	34
Completed	0	0	0
Not completed	50	65	34
Adverse event, serious fatal	-	3	1
Consent withdrawn by subject	4	3	5
Physician decision	2	4	1
Adverse event, non-fatal	6	8	6
Disease Progression	38	46	21

Protocol deviation	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Phase 1: LY2603618 + Gemcitabine

Reporting group description:

All participants in Phase 1 received LY2603618 in combination with gemcitabine.

LY2603618: 70 to 250 milligrams/meter squared (mg/m^2) LY2603618 as a 1-hour continuous intravenous (IV) infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received LY2603618 as part of the dose escalation cohort of Phase 1 (dose of 70, 105, 150, 200, or 250 mg/m^2) or as part of the expansion cohort of Phase 1 (flat dose of 200 or 230 mg). The flat dose cohorts were conducted in parallel.

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Reporting group title	Phase 2: LY2603618 + Gemcitabine

Reporting group description:

LY2603618: 230 mg flat dose LY2603618 as a 1-hour continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.
Gemcitabine: Participants were administered 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Reporting group title	Phase 2: Gemcitabine

Reporting group description:

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Reporting group values	Phase 1: LY2603618 + Gemcitabine	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine
Number of subjects	50	65	34
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	29	35	16
From 65-84 years	21	30	17
85 years and over	0	0	1
Age Continuous Units: years			
arithmetic mean	59	64.3	64.4
standard deviation	± 12.2	± 8.3	± 10.1
Gender, Male/Female Units:			
Female	24	23	14

Male	26	42	20

Race/Ethnicity, Customized Units: Subjects			
White	46	62	32
Black or African American	1	2	2
American Indian or Alaska Native	0	1	0
Asian	3	0	0
Region of Enrollment Units: Subjects			
United States	32	27	14
Spain	18	12	5
Romania	0	2	1
Germany	0	17	9
Netherlands	0	3	2
Italy	0	3	2
Poland	0	1	1
Initial Pathological Diagnosis Units: Subjects			
Adenocarcinoma, Pancreas	10	65	34
Adenocarcinoma, Colon	7	0	0
Carcinoma, Breast	4	0	0
Carcinoma, Non-Small Cell, Lung NOS	3	0	0
Adenocarcinoma, Cervix	2	0	0
Adenocarcinoma, Rectum	2	0	0
Carcinoma, Endometrium	2	0	0
Carcinoma, Infiltrating Ductal, Breast	2	0	0
Carcinoma, Renal Cell	2	0	0
Sarcoma, Leiomyosarcoma, Abdomen (Non-Gist)	2	0	0
Squamous Cell Carcinoma, Head and Neck	2	0	0
Ampulla of Pancreas	1	0	0
Carcinoma, Head and Neck	1	0	0
Carcinoma, Ovarian	1	0	0
Carcinoma, Peritoneal	1	0	0
Carcinoma, Small Cell, Lung	1	0	0
Carcinoma, Transitional Cell, Urothelium	1	0	0
Ewing's Sarcoma	1	0	0
Lymphoma, Non-Hodgkin's Lymphoma	1	0	0
Mesothelioma, Pleural, Malignant	1	0	0
Ovarian Adenocarcinoma	1	0	0
Squamous Cell Carcinoma, Cervix	1	0	0
Tumor	1	0	0
Eastern Cooperative Oncology Group (ECOG) Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status classifies participants according to their functional impairment. Scores range from 0 (Fully Active) to 5 (Death) as follows: 0 - Fully Active; 1 - Ambulatory, Restricted Strenuous Activity; 2 - Ambulatory, No			

Work Activities; 3 - Partially Confined to Bed, Limited Self Care; 4 - Completely Disabled; and 5 - Dead.			
Units: Subjects			
ECOG Status 0	19	28	14
ECOG Status 1	31	31	17
ECOG Status 2	0	6	3

Reporting group values	Total		
Number of subjects	149		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	80		
From 65-84 years	68		
85 years and over	1		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units:			
Female	61		
Male	88		
Race/Ethnicity, Customized			
Units: Subjects			
White	140		
Black or African American	5		
American Indian or Alaska Native	1		
Asian	3		
Region of Enrollment			
Units: Subjects			
United States	73		
Spain	35		
Romania	3		
Germany	26		
Netherlands	5		
Italy	5		
Poland	2		
Initial Pathological Diagnosis			
Units: Subjects			
Adenocarcinoma, Pancreas	109		
Adenocarcinoma, Colon	7		
Carcinoma, Breast	4		
Carcinoma, Non-Small Cell, Lung NOS	3		
Adenocarcinoma, Cervix	2		

Adenocarcinoma, Rectum	2		
Carcinoma, Endometrium	2		
Carcinoma, Infiltrating Ductal, Breast	2		
Carcinoma, Renal Cell	2		
Sarcoma, Leiomyosarcoma, Abdomen (Non-Gist)	2		
Squamous Cell Carcinoma, Head and Neck	2		
Ampulla of Pancreas	1		
Carcinoma, Head and Neck	1		
Carcinoma, Ovarian	1		
Carcinoma, Peritoneal	1		
Carcinoma, Small Cell, Lung	1		
Carcinoma, Transitional Cell, Urothelium	1		
Ewing's Sarcoma	1		
Lymphoma, Non-Hodgkin's Lymphoma	1		
Mesothelioma, Pleural, Malignant	1		
Ovarian Adenocarcinoma	1		
Squamous Cell Carcinoma, Cervix	1		
Tumor	1		
Eastern Cooperative Oncology Group (ECOG) Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status classifies participants according to their functional impairment. Scores range from 0 (Fully Active) to 5 (Death) as follows: 0 - Fully Active; 1 - Ambulatory, Restricted Strenuous Activity; 2 - Ambulatory, No Work Activities; 3 - Partially Confined to Bed, Limited Self Care; 4 - Completely Disabled; and 5 - Dead.			
Units: Subjects			
ECOG Status 0	61		
ECOG Status 1	79		
ECOG Status 2	9		

End points

End points reporting groups

Reporting group title	Phase 1: LY2603618 + Gemcitabine

Reporting group description:

All participants in Phase 1 received LY2603618 in combination with gemcitabine.

LY2603618: 70 to 250 milligrams/meter squared (mg/m^2) LY2603618 as a 1-hour continuous intravenous (IV) infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received LY2603618 as part of the dose escalation cohort of Phase 1 (dose of 70, 105, 150, 200, or 250 mg/m^2) or as part of the expansion cohort of Phase 1 (flat dose of 200 or 230 mg). The flat dose cohorts were conducted in parallel.

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Reporting group title	Phase 2: LY2603618 + Gemcitabine

Reporting group description:

LY2603618: 230 mg flat dose LY2603618 as a 1-hour continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.
Gemcitabine: Participants were administered 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Reporting group title	Phase 2: Gemcitabine

Reporting group description:

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Primary: Phase 1: Determine the recommended Phase 2 dose for LY2603618 when administered after gemcitabine

End point title	Phase 1: Determine the recommended Phase 2 dose for LY2603618 when administered after gemcitabine[1][2]

End point description:

The recommended Phase 2 dose for LY2603618 when administered approximately 24 hours after gemcitabine was based on the maximum tolerated dose and achievement of predefined LY2603618 plasma systemic exposures targets (area under the LY2603618 plasma concentration versus time curve from time zero to infinity [AUC(0-inf)] >21,000 nanogram*hour/milliliter [ng*h/mL] and maximum LY2603618 plasma concentration [Cmax] >2000 nanograms/milliliter [ng/mL]). Population analyzed was all phase 1 participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline through 18 months

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: Statistics are being reported for only phase 1 participants as per the protocol or Statistical Analysis Plan or both.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are being reported for only phase 1 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 1: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: milligrams (mg)				
number (not applicable)	230			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS)[3]

End point description:

Overall survival (OS) time is defined as the time from the date of randomization to the date of death from any cause. For participants not known to have died as of the data cut-off date, OS time was censored at the last contact date the participant was known to be alive prior to the cut-off date. OS was summarized using Kaplan-Meier estimates. Population analyzed was all phase 2 participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Phase 2: Baseline to date of death

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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	34		
Units: months				
median (confidence interval 95%)	7.8 (5 to 11.1)	8.3 (5.1 to 14.1)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Phase 2: LY2603618 + Gemcitabine v Phase 2: Gemcitabine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.333 [4]
Method	Bayesian Posterior Probability

Notes:

[4] - Inference about survival was made using a Bayesian posterior probability. The combination treatment would have been considered superior to gemcitabine alone if the posterior probability of superiority exceeded 0.8.

Secondary: Phase 1: Maximum Plasma Concentration (Cmax) of gemcitabine, 2',2'-difluorodeoxyuridine (dFdU), and LY2603618

End point title	Phase 1: Maximum Plasma Concentration (Cmax) of gemcitabine, 2',2'-difluorodeoxyuridine (dFdU), and LY2603618[5]

End point description:

Plasma samples for pharmacokinetic (PK) analysis were collected following IV infusion of each study drug. However, the dose-normalized PK analysis of gemcitabine and dFdU were not reported because the gemcitabine and dFdU plasma concentration data generated for all participants with PK samples collected in this study were withdrawn (invalidated) as a result of the failure of the Incurred Sample Reanalysis (ISR) for both gemcitabine and dFdU. Therefore, only the LY2603618 plasma Cmax values are reported for each LY2603618 dose level on Cycle (C) 1 /Day (D) 1, Cycle 1 /Day 16, and Cycle 2 /Day 2. The number of PK observations (n) used in the analysis is presented for each dose level and time point. Population analyzed was all phase 1 participants who received at least 1 dose of study drug and had sufficient LY2603618 plasma concentration data to enable determination of the LY2603618 Cmax.

End point type	Secondary

End point timeframe:

Phase 1: LY2603618 - Predose and 0, 1, 3, 6, 24, 48, and 72 hours after the end of infusion on C1 /D2, C1 /D16, and C2 /D2. Gemcitabine - Predose and 0, 10, 30, 60, and 120 minutes after the end of infusion on C1 /D1, C1 /D15, and C2 /D1.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are being reported for only phase 1 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 1: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
70 mg/m^2, Cycle 1 /Day 2 (n=2)	3530 (± 23)			
70 mg/m^2, Cycle 1 /Day 16 (n=3)	3360 (± 26)			
70 mg/m^2, Cycle 2 /Day 2 (n=3)	3100 (± 12)			
105 mg/m^2, Cycle 1 /Day 2 (n=3)	4890 (± 25)			
105 mg/m^2, Cycle 1 /Day 16 (n=3)	5170 (± 38)			
105 mg/m^2, Cycle 2 /Day 2 (n=3)	5360 (± 23)			
150 mg/m^2, Cycle 1 /Day 2 (n=7)	4280 (± 29)			
150 mg/m^2, Cycle 1 /Day 16 (n=6)	5040 (± 38)			
150 mg/m^2, Cycle 2 /Day 2 (n=6)	4370 (± 38)			
200 mg/m^2, Cycle 1 /Day 2 (n=11)	4870 (± 63)			
200 mg/m^2, Cycle 1 /Day 16 (n=8)	5360 (± 40)			
200 mg/m^2, Cycle 2 /Day 2 (n=11)	5290 (± 40)			
250 mg/m^2, Cycle 1 /Day 2 (n=5)	7990 (± 25)			
250 mg/m^2, Cycle 1 /Day 16 (n=3)	7990 (± 6)			
250 mg/m^2, Cycle 2 /Day 2 (n=3)	5290 (± 35)			
200 mg (flat dose), Cycle 1 /Day 2 (n=10)	3440 (± 65)			
200 mg (flat dose), Cycle 1 /Day 16 (n=6)	3470 (± 61)			

200 mg (flat dose), Cycle 2 /Day 2 (n=8)	3640 (± 45)			
230 mg (flat dose), Cycle 1 /Day 2 (n=10)	4820 (± 72)			
230 mg (flat dose), Cycle 1 /Day 16 (n=6)	4980 (± 35)			
230 mg (flat dose), Cycle 2 /Day 2 (n=7)	3830 (± 26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Plasma Concentration versus Time Curve (AUC) of gemcitabine, dFdU, and LY2603618

End point title	Phase 1: Area Under the Plasma Concentration versus Time Curve (AUC) of gemcitabine, dFdU, and LY2603618[6]

End point description:

Plasma samples for PK analysis were collected following IV infusion of each study drug. However, the dose-normalized PK analysis of gemcitabine and dFdU were not reported because the gemcitabine plasma and dFdU concentration data generated for all pts. with PK samples collected in this study were withdrawn (invalidated) as a result of failure of Incurred Sample Reanalysis (ISR) for both gemcitabine and dFdU. Therefore, only study drug plasma AUC from time zero to 24 hours (AUC[0-24]), AUC from time zero to last time point with measurable concentration (AUC[0-tlast]), and AUC from time zero to infinity (AUC[0-inf]) values are reported for each study drug dose level on Cycle1/Day1, Cycle1/Day16, and Cycle2/Day2. The number of PK observations (n) used in the analysis is presented for each dose level and time point. Population analyzed was all phase 1 pts. who received at least 1 dose of study drug and had sufficient study drug plasma concentration to enable calculation of study drug AUC.

End point type	Secondary

End point timeframe:

Phase 1: LY2603618 - Predose and 0, 1, 3, 6, 24, 48, and 72 hours after the end of infusion on C1 /D2, C1 /D16, and C2 /D2. Gemcitabine - Predose and 0, 10, 30, 60, and 120 minutes after the end of infusion on C1 /D1, C1 /D15, and C2 /D1.

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: Statistics are being reported for only phase 1 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 1: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: nanogram*hour/milliliter (ng*h/mL)				
geometric mean (geometric coefficient of variation)				
AUC(0-24), 70 mg/m^2, Cycle 1 /Day 2 (n=2)	21300 (± 24)			
AUC(0-24), 70 mg/m^2, Cycle 1 /Day 16 (n=3)	21200 (± 27)			
AUC(0-24), 70 mg/m^2, Cycle 2 /Day 2 (n=3)	19900 (± 24)			
AUC(0-24), 105 mg/m^2, Cycle 1 /Day 2 (n=3)	40500 (± 23)			
AUC(0-24), 105 mg/m^2, Cycle 1 /Day 16 (n=3)	50100 (± 32)			

AUC(0-24), 105 mg/m^2, Cycle 2 /Day 2 (n=3)	49800 (± 4)			
AUC(0-24), 150 mg/m^2, Cycle 1 /Day 2 (n=7)	32200 (± 27)			
AUC(0-24), 150 mg/m^2, Cycle 1 /Day 16 (n=6)	40000 (± 29)			
AUC(0-24), 150 mg/m^2, Cycle 2 /Day 2 (n=6)	31000 (± 42)			
AUC(0-24), 200 mg/m^2, Cycle 1 /Day 2 (n=10)	40200 (± 42)			
AUC(0-24), 200 mg/m^2, Cycle 1 /Day 16 (n=8)	39800 (± 36)			
AUC(0-24), 200 mg/m^2, Cycle 2 /Day 2 (n=11)	44300 (± 39)			
AUC(0-24), 250 mg/m^2, Cycle 1 /Day 2 (n=5)	88800 (± 27)			
AUC(0-24), 250 mg/m^2, Cycle 1 /Day 16 (n=3)	61000 (± 63)			
AUC(0-24), 250 mg/m^2, Cycle 2 /Day 2 (n=3)	40000 (± 112)			
AUC(0-24), 200 mg (flat), Cycle 1 /Day 2 (n=10)	22900 (± 77)			
AUC(0-24), 200 mg (flat), Cycle 1 /Day 16 (n=6)	28700 (± 63)			
AUC(0-24), 200 mg (flat), Cycle 2 /Day 2 (n=8)	23800 (± 62)			
AUC(0-24), 230 mg (flat), Cycle 1 /Day 2 (n=10)	32400 (± 38)			
AUC(0-24), 230 mg (flat), Cycle 1 /Day 16 (n=6)	32300 (± 22)			
AUC(0-24), 230 mg (flat), Cycle 2 /Day 2 (n=7)	32500 (± 24)			
AUC(0-tlast), 70 mg/m^2, Cycle 1 /Day 2 (n=2)	24600 (± 28)			
AUC(0-tlast), 70 mg/m^2, Cycle 1 /Day 16 (n=3)	27500 (± 21)			
AUC(0-tlast), 70 mg/m^2, Cycle 2 /Day 2 (n=3)	25800 (± 29)			
AUC(0-tlast), 105 mg/m^2, Cycle 1 /Day 2 (n=3)	65800 (± 53)			
AUC(0-tlast), 105 mg/m^2, Cycle 1 /Day 16 (n=3)	75500 (± 46)			
AUC(0-tlast), 105 mg/m^2, Cycle 2 /Day 2 (n=3)	79600 (± 19)			
AUC(0-tlast), 150 mg/m^2, Cycle 1 /Day 2 (n=7)	41600 (± 31)			
AUC(0-tlast), 150 mg/m^2, Cycle 1 /Day 16 (n=6)	52000 (± 38)			
AUC(0-tlast), 150 mg/m^2, Cycle 2 /Day 2 (n=6)	39800 (± 45)			
AUC(0-tlast), 200 mg/m^2, Cycle 1 /Day 2 (n=11)	44300 (± 85)			
AUC(0-tlast), 200 mg/m^2, Cycle 1 /Day 16 (n=8)	55300 (± 51)			
AUC(0-tlast), 200 mg/m^2, Cycle 2 /Day 2 (n=11)	55600 (± 51)			
AUC(0-tlast), 250 mg/m^2, Cycle 1 /Day 2 (n=5)	140000 (± 37)			
AUC(0-tlast), 250 mg/m^2, Cycle 1 /Day 16 (n=3)	98200 (± 139)			
AUC(0-tlast), 250 mg/m^2, Cycle 2 /Day 2 (n=3)	60400 (± 178)			

AUC(0-tlast), 200 mg (flat), Cycle 1 /Day 2 (n=10)	33100 (± 101)			
AUC(0-tlast), 200 mg (flat), Cycle 1 /Day 16 (n=6)	42600 (± 88)			
AUC(0-tlast), 200 mg (flat), Cycle 2 /Day 2 (n=8)	32400 (± 85)			
AUC(0-tlast), 230 mg (flat), Cycle 1 /Day 2 (n=10)	43000 (± 50)			
AUC(0-tlast), 230 mg (flat), Cycle 1 /Day 16 (n=6)	51900 (± 50)			
AUC(0-tlast), 230 mg (flat), Cycle 2 /Day 2 (n=7)	45900 (± 26)			
AUC(0-inf), 70 mg/m^2, Cycle 1 /Day 2 (n=2)	24900 (± 29)			
AUC(0-inf), 70 mg/m^2, Cycle 1 /Day 16 (n=3)	28600 (± 19)			
AUC(0-inf), 70 mg/m^2, Cycle 2 /Day 2 (n=3)	27100 (± 31)			
AUC(0-inf), 105 mg/m^2, Cycle 1 /Day 2 (n=3)	78600 (± 68)			
AUC(0-inf), 105 mg/m^2, Cycle 1 /Day 16 (n=3)	79800 (± 51)			
AUC(0-inf), 105 mg/m^2, Cycle 2 /Day 2 (n=3)	88800 (± 25)			
AUC(0-inf), 150 mg/m^2, Cycle 1 /Day 2 (n=7)	42800 (± 33)			
AUC(0-inf), 150 mg/m^2, Cycle 1 /Day 16 (n=6)	54600 (± 43)			
AUC(0-inf), 150 mg/m^2, Cycle 2 /Day 2 (n=6)	41000 (± 46)			
AUC(0-inf), 200 mg/m^2, Cycle 1 /Day 2 (n=10)	60300 (± 58)			
AUC(0-inf), 200 mg/m^2, Cycle 1 /Day 16 (n=8)	56800 (± 54)			
AUC(0-inf), 200 mg/m^2, Cycle 2 /Day 2 (n=11)	65400 (± 49)			
AUC(0-inf), 250 mg/m^2, Cycle 1 /Day 2 (n=5)	153000 (± 41)			
AUC(0-inf), 250 mg/m^2, Cycle 1 /Day 16 (n=3)	101000 (± 141)			
AUC(0-inf), 250 mg/m^2, Cycle 2 /Day 2 (n=3)	70500 (± 216)			
AUC(0-inf), 200 mg (flat), Cycle 1 /Day 2 (n=10)	35200 (± 117)			
AUC(0-inf), 200 mg (flat), Cycle 1 /Day 16 (n=6)	45700 (± 93)			
AUC(0-inf), 200 mg (flat), Cycle 2 /Day 2 (n=8)	34400 (± 93)			
AUC(0-inf), 230 mg (flat), Cycle 1 /Day 2 (n=10)	45200 (± 50)			
AUC(0-inf), 230 mg (flat), Cycle 1 /Day 16 (n=6)	57700 (± 58)			
AUC(0-inf), 230 mg (flat), Cycle 2 /Day 2 (n=7)	48000 (± 26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Maximum Plasma Concentration (Cmax) of gemcitabine, dFdU, and LY2603618

End point title	Phase 2: Maximum Plasma Concentration (Cmax) of gemcitabine, dFdU, and LY2603618[7]

End point description:

Plasma samples for PK analysis were collected following IV infusion of each study drug. However, the dose-normalized PK analysis of gemcitabine and dFdU were not reported because the gemcitabine and dFdU plasma concentration data generated for all participants with PK samples collected in this study were withdrawn (invalidated) as a result of the failure of the Incurred Sample Reanalysis (ISR) for both gemcitabine and dFdU. Therefore, only the LY2603618 plasma Cmax values are reported at the 230 mg LY2603618 dose level on Cycle 1 /Day 1, Cycle 1 /Day 16, and Cycle 2 /Day 2. The number of PK observations (n) used in the analysis is presented for each time point. Population analyzed was all phase 2 participants who received at least 1 dose of study drug and had sufficient LY2603618 plasma concentration data to enable determination of the LY2603618 Cmax.

End point type	Secondary

End point timeframe:

Phase 2: LY2603618 - Predose and 0, 1, 3, and 24 hours after the end of infusion on Days 2 and 16 of Cycle 1. Gemcitabine - Predose and 0, 10, 60, and 120 minutes after the end of infusion on Days 1 and 15 of Cycle 1.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 /Day 2 (n=58)	3170 (± 50)			
Cycle 1 /Day 16 (n=48)	3410 (± 50)			
Cycle 2 /Day 2 (n=2)	2390 (± 54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression-free Survival (PFS)

End point title	Phase 2: Progression-free Survival (PFS)[8]

End point description:

Progression-free survival (PFS) time was defined as the time from the date of randomization to the first date of progressive disease (symptomatic or objective) or death due to any cause, whichever occurred first. For participants who were not known to have died or progressed as of the data-inclusion cutoff date, PFS time was censored at the date of the last objective progression-free disease assessment prior to the date of any subsequent systematic anticancer therapy. PFS was summarized using Kaplan-Meier estimates. Population analyzed was all phase 2 participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Phase 2: Baseline to measured progressive disease or date of death from any cause

Notes:

[8] - 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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	34		
Units: months				
median (confidence interval 95%)	3.5 (2.1 to 3.6)	5.6 (2.6 to 7.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Area Under the Plasma Concentration versus Time Curve (AUC) of gemcitabine, dFdU, and LY2603618

End point title	Phase 2: Area Under the Plasma Concentration versus Time Curve (AUC) of gemcitabine, dFdU, and LY2603618[9]

End point description:

Plasma samples for PK analysis were collected following IV infusion of each study drug. However, the dose-normalized PK analysis of gemcitabine and dFdU were not reported because the gemcitabine and dFdU plasma concentration data generated for all participants with PK samples collected in this study were withdrawn (invalidated) as a result of the failure of the Incurred Sample Reanalysis (ISR) for both gemcitabine and dFdU. Therefore, only the LY2603618 plasma AUC(0-24), AUC(0-tlast), and AUC(0-inf) values are reported for the 230 mg LY2603618 dose on Cycle 1 /Day 1, Cycle 1 /Day 16, and Cycle 2 /Day 2. The number of PK observations (n) used in the analysis is presented for each time point. Population analyzed was all phase 2 participants who received at least 1 dose of study drug and had sufficient LY2603618 plasma concentration data to enable calculation of the LY2603618 AUC.

End point type	Secondary

End point timeframe:

Phase 2: LY2603618 - Predose and 0, 1, 3, and 24 hours after the end of infusion on Days 2 and 16 of Cycle 1. Gemcitabine - Predose and 0, 10, 60, and 120 minutes after the end of infusion on Days 1 and 15 of Cycle 1.

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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
AUC(0-24), Cycle 1 /Day 2 (n=54)	23200 (± 68)			
AUC(0-24), Cycle 1 /Day 16 (n=42)	23700 (± 60)			
AUC(0-24), Cycle 2 /Day 2 (n=2)	19800 (± 63)			
AUC(0-tlast), Cycle 1 /Day 2 (n=58)	22200 (± 73)			
AUC(0-tlast), Cycle 1 /Day 16 (n=48)	20800 (± 78)			

AUC(0-tlast), Cycle 2 /Day 2 (n=2)	20100 (± 64)			
AUC(0-inf), Cycle 1 /Day 2 (n=54)	29400 (± 84)			
AUC(0-inf), Cycle 1 /Day 16 (n=42)	29100 (± 74)			
AUC(0-inf), Cycle 2 /Day 2 (n=2)	23300 (± 69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Response Rate

End point title	Phase 2: Overall Response Rate[10]

End point description:

Overall response rate is the best response of complete response (CR) or partial response (PR) as classified by the investigators according to the Response Evaluation Criteria In Solid Tumors (RECIST v1.1) guidelines. CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of not-target lesions or appearance of new lesions. Overall response rate is calculated as a total number of participants with CR or PR divided by the total number of participants with at least 1 measurable lesion, multiplied by 100. Population analyzed was all phase 2 participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Phase 2: Baseline to measured progressive disease or date of death from any cause

Notes:

[10] - 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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	34		
Units: percentage of participants				
number (confidence interval 95%)	21.5 (12.3 to 33.5)	8.8 (1.9 to 23.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Clinical Benefit Rate

End point title	Phase 2: Clinical Benefit Rate[11]

End point description:

Clinical benefit rate is the best response CR, PR, or stable disease (SD) as classified by the investigators according to the RECIST v1.1 guidelines. CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of not-target lesions or appearance of new lesions. SD is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum diameter since treatment

started. Overall response rate is calculated as a total number of participants with CR, PR, or SD divided by the total number of participants with at least 1 measurable lesion, multiplied by 100. Population analyzed was all phase 2 participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Phase 2: Baseline to measured progressive disease or date of death from any cause

Notes:

[11] - 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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	34		
Units: percentage of participants				
number (confidence interval 95%)	55.4 (42.5 to 67.7)	64.7 (46.5 to 80.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response

End point title	Phase 2: Duration of Response[12]

End point description:

Duration of response was defined as the time from the first observation of complete response (CR) or partial response (PR) to the first observation of progressive disease or death from any cause. For participants who were not known to have died as of the data-inclusion cut-off date and who do not have progressive disease, the duration was censored at the date of the last objective progression-free disease assessment prior to the date of any subsequent anticancer therapy (systemic, radiologic, or surgery). Participants were also censored at the last valid assessment prior to missing more than 1 consecutive scheduled assessment. Duration of response was summarized using Kaplan-Meier estimates. Population analyzed was all phase 2 participants who received at least 1 dose of study drug and had a confirmed response (CR or PR).

End point type	Secondary

End point timeframe:

Phase 2. Baseline to measured progressive disease or date of death from any cause

Notes:

[12] - 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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	3		
Units: months				
median (confidence interval 95%)	3.5 (1.9 to 5.8)	6 (3.7 to 6.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Electrocardiogram QTc Prolongation

End point title	Phase 2: Electrocardiogram QTc Prolongation[13]

End point description:

The QT interval is a measure of the time between the start of the Q wave and the end of the T wave. Twelve-lead ECG data was used to calculate QTc based on Fridericia's formula (QTc=QT/RR^0.33, where RR is the interval between two R waves). For each participant, changes in QTc were calculated by subtracting the reading taken before LY2603618 administration from the reading taken after LY2603618 administration on Days 2 and 16 during Cycle 1. The number of participants in which the change in QTc was <=30 milliseconds (msec), >30-60 msec, or >60 msec is presented. Population analyzed was all phase 2 participants who received at least 1 dose of study drug and had evaluable ECG data.

End point type	Secondary

End point timeframe:

Phase 2: Days 2 and 16 of Cycle 1

Notes:

[13] - 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: Statistics are being reported for only phase 2 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 2: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: participants				
number (not applicable)				
<=30 msec	55			
>30-60 msec	5			
>60 msec	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Electrocardiogram QTc prolongation

End point title	Phase 1: Electrocardiogram QTc prolongation[14]

End point description:

The QT interval is a measure of the time between the start of the Q wave and the end of the T wave. Twelve-lead electrocardiogram (ECG) data was used to calculate the corrected QT (QTc) based on Fridericia's formula (QTc=QT/RR^0.33, where RR is the interval between two R waves). For each participant, changes in QTc were calculated by subtracting the reading taken before LY2603618 administration from the reading taken after LY2603618 administration on Days 2 and 16 during Cycle 1.

The number of participants in which the change in QTc was <=30 milliseconds (msec), >30-60 msec, or >60 msec is presented by dose group and overall. Population analyzed was all phase 1 participants who received at least 1 dose of study drug and had evaluable ECG data.

End point type	Secondary

End point timeframe:

Phase 1: Days 2 and 16 of Cycle 1

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: Statistics are being reported for only phase 1 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 1: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: participants				
number (not applicable)				
70 mg/m^2, <=30 msec (n=3)	2			
70 mg/m^2, >30-60 msec (n=3)	1			
70 mg/m^2, >60 msec (n=3)	0			
105 mg/m^2, <=30 msec (n=3)	2			
105 mg/m^2, >30-60 msec (n=3)	0			
105 mg/m^2, >60 msec (n=3)	0			
150 mg/m^2, <=30 msec (n=7)	6			
150 mg/m^2, >30-60 msec (n=7)	1			
150 mg/m^2, >60 msec (n=7)	0			
200 mg/m^2, <=30 msec (n=11)	11			
200 mg/m^2, >30-60 msec (n=11)	0			
200 mg/m^2, >60 msec (n=11)	0			
250 mg/m^2, <=30 msec (n=6)	6			
250 mg/m^2, >30-60 msec (n=6)	0			
250 mg/m^2, >60 msec (n=6)	0			
200 mg (flat dose), <=30 msec (n=10)	9			
200 mg (flat dose), >30-60 msec (n=10)	1			
200 mg (flat dose), >60 msec (n=10)	0			
230 mg (flat dose), <=30 msec (n=10)	8			
230 mg (flat dose), >30-60 msec (n=10)	2			
230 mg (flat dose), >60 msec (n=10)	0			
Total, <=30 msec	44			
Total, >30-60 msec	5			
Total, >60 msec	0			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Deaths During the Phase 1 Post-study Period

End point title	Number of Deaths During the Phase 1 Post-study Period[15]

End point description:

The number of participants who died during the post-study period of Phase 1 does not include the outcomes for the 4 participants who died while on treatment during Phase 2 as captured in the Participant Flow Table. A summary of serious and other nonserious adverse events regardless of causality is located in the Reported Adverse Events module. Population analyzed was all phase 1 participants who received at least 1 dose of study drug.

End point type	Other pre-specified

End point timeframe:

Phase 1: Time of last dose of study drug through the end of the follow-up period

Notes:

[15] - 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: Statistics are being reported for only phase 1 participants as per the protocol or Statistical Analysis Plan or both.

End point values	Phase 1: LY2603618 + Gemcitabine			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: participants				
number (not applicable)				
Total deaths	5			
Deaths within 30 days of last dose of study drug	4			
Deaths during the follow-up period	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

I2I-MC-JMMC

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Phase 1

Reporting group description:

All participants in Phase 1 received LY2603618 in combination with gemcitabine.

LY2603618: 70 to 250 mg/m^2 LY2603618 as a 1-hour continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received LY2603618 as part of the dose escalation cohort of Phase 1 (dose of 70, 105, 150, 200, or 250 mg/m^2) or as part of the expansion cohort of Phase 1 (flat dose of 200 or 230 mg). The flat dose cohorts were conducted in parallel.

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Reporting group title	Phase 2: LY2603618 + Gemcitabine

Reporting group description:

LY2603618: 230 mg flat dose LY2603618 as a 1-hour continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Gemcitabine: Participants were administered 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression. Participants received gemcitabine 24 hours prior to LY2603618 administration.

Reporting group title	Phase 2: Gemcitabine

Reporting group description:

Gemcitabine: 1000 mg/m^2 gemcitabine as a 30-minute continuous IV infusion once per week for 3 weeks, followed by 1 week of rest. This 28-day cycle was repeated for a minimum of 2 cycles and/or until disease progression.

Serious adverse events	Phase 1	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 50 (42.00%)	27 / 65 (41.54%)	18 / 34 (52.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
malignant ascites			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metastases to ovary			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed[1]	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tumour pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypotension			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
phlebitis			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
phlebitis superficial			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
venous thrombosis limb			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
device occlusion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fatigue			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	3 / 65 (4.62%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombosis in device			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
acute pulmonary oedema			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (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
acute respiratory failure			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
interstitial lung disease			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonitis			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
c-reactive protein increased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
international normalised ratio increased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
infusion related reaction			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
angina pectoris			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bundle branch block left			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (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
left ventricular dysfunction			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (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
myocardial infarction			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (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
syncope			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disseminated intravascular coagulation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemolytic uraemic syndrome			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhagic anaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutropenia			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	2 / 50 (4.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombotic microangiopathy			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ascites			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colitis ischaemic			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
constipation			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	1 / 50 (2.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
duodenal ulcer perforation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus paralytic			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal ischaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal obstruction			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

nausea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatic pseudocyst			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
small intestinal obstruction			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (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
vomiting			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	2 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
bile duct obstruction			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholangitis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	3 / 65 (4.62%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholestasis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
jaundice			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
nephrotic syndrome			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureteric stenosis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
abdominal sepsis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
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 15.1			
subjects affected / exposed	1 / 50 (2.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bacterial sepsis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bronchitis			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clostridium difficile colitis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
device related infection			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
escherichia bacteraemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal abscess			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

sepsis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dehydration			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyperkalaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypovolaemia			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

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

Non-serious adverse events	Phase 1	Phase 2: LY2603618 + Gemcitabine	Phase 2: Gemcitabine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 50 (96.00%)	64 / 65 (98.46%)	34 / 34 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
tumour pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	3
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	4 / 65 (6.15%)	3 / 34 (8.82%)
occurrences (all)	1	4	3
flushing			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	6 / 50 (12.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences (all)	8	0	0
hypertension			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	3 / 65 (4.62%)	3 / 34 (8.82%)
occurrences (all)	1	3	3
hypotension			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	3 / 65 (4.62%)	5 / 34 (14.71%)
occurrences (all)	5	3	5
thrombophlebitis superficial			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	4 / 65 (6.15%)	0 / 34 (0.00%)
occurrences (all)	0	4	0
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	10 / 65 (15.38%)	5 / 34 (14.71%)
occurrences (all)	5	19	8
chills			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	9 / 65 (13.85%)	2 / 34 (5.88%)
occurrences (all)	6	15	2
fatigue			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	31 / 50 (62.00%)	22 / 65 (33.85%)	14 / 34 (41.18%)
occurrences (all)	50	28	19
influenza like illness			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	3 / 65 (4.62%)	3 / 34 (8.82%)
occurrences (all)	3	8	3
infusion site pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences (all)	10	0	4
irritability			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences (all)	3	0	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences (all)	3	1	1
oedema peripheral			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	8 / 50 (16.00%)	19 / 65 (29.23%)	12 / 34 (35.29%)
occurrences (all)	9	23	16
pyrexia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	15 / 50 (30.00%)	19 / 65 (29.23%)	11 / 34 (32.35%)
occurrences (all)	33	23	14
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences (all)	5	5	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	10 / 50 (20.00%)	7 / 65 (10.77%)	5 / 34 (14.71%)
occurrences (all)	12	7	6
dysphonia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	2 / 34 (5.88%)
occurrences (all)	0	2	2
dyspnoea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	8 / 50 (16.00%)	12 / 65 (18.46%)	2 / 34 (5.88%)
occurrences (all)	11	13	2
dyspnoea exertional			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	2 / 65 (3.08%)	1 / 34 (2.94%)
occurrences (all)	7	2	1
epistaxis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	5	2	0
Psychiatric disorders			

anxiety			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	0 / 65 (0.00%)	3 / 34 (8.82%)
occurrences (all)	4	0	3
confusional state			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	1 / 65 (1.54%)	2 / 34 (5.88%)
occurrences (all)	1	1	2
depression			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	6 / 50 (12.00%)	2 / 65 (3.08%)	3 / 34 (8.82%)
occurrences (all)	7	2	4
insomnia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	7 / 50 (14.00%)	4 / 65 (6.15%)	6 / 34 (17.65%)
occurrences (all)	9	4	8
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	10 / 50 (20.00%)	13 / 65 (20.00%)	6 / 34 (17.65%)
occurrences (all)	15	18	6
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	11 / 50 (22.00%)	10 / 65 (15.38%)	5 / 34 (14.71%)
occurrences (all)	14	15	5
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	5 / 65 (7.69%)	3 / 34 (8.82%)
occurrences (all)	0	5	3
blood lactate dehydrogenase increased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	2 / 65 (3.08%)	3 / 34 (8.82%)
occurrences (all)	1	2	3
gamma-glutamyltransferase increased			

alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	12 / 65 (18.46%)	3 / 34 (8.82%)
occurrences (all)	4	12	3
haemoglobin decreased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	2 / 34 (5.88%)
occurrences (all)	0	2	3
neutrophil count decreased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	3 / 65 (4.62%)	2 / 34 (5.88%)
occurrences (all)	0	3	6
platelet count decreased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	7 / 65 (10.77%)	1 / 34 (2.94%)
occurrences (all)	0	11	5
weight decreased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	7 / 65 (10.77%)	3 / 34 (8.82%)
occurrences (all)	3	8	3
white blood cell count decreased			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	2 / 65 (3.08%)	2 / 34 (5.88%)
occurrences (all)	2	4	8
Injury, poisoning and procedural complications			
infusion related reaction			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	3	1	0
procedural pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences (all)	4	0	0
Cardiac disorders			

sinus tachycardia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	1
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	5 / 65 (7.69%)	4 / 34 (11.76%)
occurrences (all)	5	5	4
dysgeusia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	5 / 65 (7.69%)	2 / 34 (5.88%)
occurrences (all)	5	5	2
headache			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	7 / 65 (10.77%)	2 / 34 (5.88%)
occurrences (all)	7	10	2
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	7 / 65 (10.77%)	2 / 34 (5.88%)
occurrences (all)	4	8	4
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	23 / 50 (46.00%)	16 / 65 (24.62%)	10 / 34 (29.41%)
occurrences (all)	29	21	13
leukocytosis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	3	1	0
leukopenia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	8 / 65 (12.31%)	6 / 34 (17.65%)
occurrences (all)	5	27	10
lymphopenia			

alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	4 / 65 (6.15%)	4 / 34 (11.76%)
occurrences (all)	6	7	4
neutropenia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	16 / 50 (32.00%)	15 / 65 (23.08%)	10 / 34 (29.41%)
occurrences (all)	26	49	24
thrombocytopenia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	23 / 50 (46.00%)	23 / 65 (35.38%)	15 / 34 (44.12%)
occurrences (all)	46	63	39
thrombocytosis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	0 / 65 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	5
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	3	2	0
abdominal distension			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	2 / 65 (3.08%)	2 / 34 (5.88%)
occurrences (all)	4	3	2
abdominal pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	12 / 50 (24.00%)	14 / 65 (21.54%)	5 / 34 (14.71%)
occurrences (all)	12	19	7
abdominal pain upper			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	5 / 65 (7.69%)	1 / 34 (2.94%)
occurrences (all)	2	5	1
anorectal discomfort			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	0 / 50 (0.00%)	0 / 65 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
constipation			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	17 / 50 (34.00%)	21 / 65 (32.31%)	9 / 34 (26.47%)
occurrences (all)	22	27	10
diarrhoea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	8 / 50 (16.00%)	21 / 65 (32.31%)	10 / 34 (29.41%)
occurrences (all)	10	36	15
dyspepsia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	4 / 65 (6.15%)	1 / 34 (2.94%)
occurrences (all)	3	4	1
flatulence			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	4 / 65 (6.15%)	0 / 34 (0.00%)
occurrences (all)	1	7	0
gastritis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	3	1	0
haemorrhoids			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	0 / 65 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
nausea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	20 / 50 (40.00%)	27 / 65 (41.54%)	15 / 34 (44.12%)
occurrences (all)	25	42	21
steatorrhoea			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	1 / 65 (1.54%)	2 / 34 (5.88%)
occurrences (all)	0	1	2

stomatitis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	13 / 65 (20.00%)	2 / 34 (5.88%)
occurrences (all)	9	14	2
vomiting			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	14 / 50 (28.00%)	19 / 65 (29.23%)	4 / 34 (11.76%)
occurrences (all)	16	35	5
Hepatobiliary disorders			
hyperbilirubinaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	2 / 65 (3.08%)	4 / 34 (11.76%)
occurrences (all)	2	2	4
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	2 / 50 (4.00%)	7 / 65 (10.77%)	5 / 34 (14.71%)
occurrences (all)	2	8	6
decubitus ulcer			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	4 / 65 (6.15%)	0 / 34 (0.00%)
occurrences (all)	1	4	0
dermatitis acneiform			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	2 / 65 (3.08%)	0 / 34 (0.00%)
occurrences (all)	5	2	0
hyperhidrosis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	3	1	0
pruritus			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	4 / 65 (6.15%)	2 / 34 (5.88%)
occurrences (all)	1	6	2
Renal and urinary disorders			

pollakiuria			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	0 / 34 (0.00%)
occurrences (all)	3	1	0
back pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	6 / 50 (12.00%)	9 / 65 (13.85%)	4 / 34 (11.76%)
occurrences (all)	6	10	4
muscular weakness			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	7 / 50 (14.00%)	2 / 65 (3.08%)	2 / 34 (5.88%)
occurrences (all)	9	2	2
musculoskeletal chest pain			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	2 / 34 (5.88%)
occurrences (all)	3	0	2
pain in extremity			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	5 / 50 (10.00%)	8 / 65 (12.31%)	1 / 34 (2.94%)
occurrences (all)	7	9	1
Infections and infestations			
oral candidiasis			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	1 / 65 (1.54%)	1 / 34 (2.94%)
occurrences (all)	4	2	1
upper respiratory tract infection			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences (all)	4	0	0
urinary tract infection			

alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	2 / 65 (3.08%)	3 / 34 (8.82%)
occurrences (all)	3	2	3
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	16 / 50 (32.00%)	21 / 65 (32.31%)	5 / 34 (14.71%)
occurrences (all)	19	22	6
dehydration			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	1 / 65 (1.54%)	3 / 34 (8.82%)
occurrences (all)	4	1	3
hyperglycaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	12 / 65 (18.46%)	4 / 34 (11.76%)
occurrences (all)	8	13	6
hyperkalaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	0 / 50 (0.00%)	2 / 65 (3.08%)	3 / 34 (8.82%)
occurrences (all)	0	2	4
hypoalbuminaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	4 / 65 (6.15%)	3 / 34 (8.82%)
occurrences (all)	2	4	3
hypocalcaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	1 / 50 (2.00%)	2 / 65 (3.08%)	6 / 34 (17.65%)
occurrences (all)	1	4	6
hypokalaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	1 / 65 (1.54%)	5 / 34 (14.71%)
occurrences (all)	4	1	6
hyponatraemia			
alternative dictionary used: MedDRA 15.1			

subjects affected / exposed	3 / 50 (6.00%)	6 / 65 (9.23%)	5 / 34 (14.71%)
occurrences (all)	4	7	5
hypovolaemia			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	4 / 50 (8.00%)	0 / 65 (0.00%)	0 / 34 (0.00%)
occurrences (all)	8	0	0
vitamin d deficiency			
alternative dictionary used: MedDRA 15.1			
subjects affected / exposed	3 / 50 (6.00%)	0 / 65 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 September 2009	Amendment (a) clarified dose omissions/reductions during a cycle, declaration of a DLT, and description of the MTD that will be carried into Phase 2. The ECG collection was also clarified.
30 June 2010	Amendment (b) added 2 additional cohorts of patients (n=20) prior to selecting the recommended Phase 2 dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported