

**Clinical trial results:****A Phase 1b/2 Dose Escalation and Cohort Expansion Study of the Safety, Tolerability and Efficacy of a Novel Transforming Growth Factor-beta Receptor I Kinase Inhibitor (Galunisertib) Administered in Combination With Anti-PD-1 (Nivolumab) in Advanced Refractory Solid Tumors (Phase 1b) and in Recurrent or Refractory Non-small Cell Lung Cancer, Hepatocellular Carcinoma, or Glioblastoma (Phase 2)****Summary**

EudraCT number	2015-002093-20
Trial protocol	DE
Global end of trial date	08 July 2020

Results information

Result version number	v2 (current)
This version publication date	03 November 2021
First version publication date	18 July 2021
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Separate cohorts for Phase 2 PK data.

Trial information**Trial identification**

Sponsor protocol code	H9H-MC-JBEF
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02423343
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15702

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	08 July 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety, tolerability, and efficacy of the study drug known as galunisertib in combination with nivolumab in participants with advanced refractory solid tumors and in recurrent or refractory non-small cell lung cancer (NSCLC) or hepatocellular carcinoma (HCC).

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	01 January 2015
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: 13
Country: Number of subjects enrolled	Spain: 28
Worldwide total number of subjects	41
EEA total number of subjects	28

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	28
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Due low enrollment, the Hepatocellular Carcinoma (HCC) cohort was terminated early.

Pre-assignment

Screening details:

Participants who had at least one post baseline tumor assessment were considered to have completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Galunisertib + Nivolumab (Cohort 1) Phase 1b

Arm description:

50 milligram (mg) Galunisertib administered orally daily (QD) on Day 1 through Day 14 of each 4-week cycle in combination with 3 milligrams per kilogram (3 mg/kg) nivolumab given intravenously (IV), every 2 weeks (Q2W), on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Arm type	Experimental
Investigational medicinal product name	Galunisertib
Investigational medicinal product code	
Other name	LY2157299
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	OPDIVO®
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Galunisertib + Nivolumab (Cohort 2) Phase 1b
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Arm description:

50 mg Galunisertib administered orally twice daily (BID) on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Arm type	Experimental
Investigational medicinal product name	Galunisertib
Investigational medicinal product code	
Other name	LY2157299
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Galunisertib + Nivolumab (Cohort 3) Phase 1b
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Arm description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Arm type	Experimental
Investigational medicinal product name	Galunisertib
Investigational medicinal product code	
Other name	LY2157299
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Galunisertib + Nivolumab (Cohort 4) Phase 1b
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Arm description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Arm type	Experimental
Investigational medicinal product name	Galunisertib
Investigational medicinal product code	
Other name	LY2157299
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Galunisertib + Nivolumab (NSCLC) Phase 2
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Arm description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Arm type	Experimental
Investigational medicinal product name	Galunisertib
Investigational medicinal product code	
Other name	LY2157299
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Galunisertib + Nivolumab (HCC) Phase 2
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Arm description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Hepatocellular Carcinoma (HCC)

Arm type	Experimental
Investigational medicinal product name	Galunisertib
Investigational medicinal product code	
Other name	LY2157299
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Number of subjects in period 1	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b
Started	3	5	3
Received at Least 1 Dose of Study Drug	3	5	3
Completed	3	4	3
Not completed	0	1	0
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-
Progressive Disease	-	-	-

Number of subjects in period 1	Galunisertib + Nivolumab (Cohort 4) Phase 1b	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2
Started	4	25	1
Received at Least 1 Dose of Study Drug	4	25	1
Completed	4	20	1
Not completed	0	5	0
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	2	-
Progressive Disease	-	2	-

Baseline characteristics

Reporting groups

Reporting group title	Galunisertib + Nivolumab (Cohort 1) Phase 1b
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Reporting group description:

50 milligram (mg) Galunisertib administered orally daily (QD) on Day 1 through Day 14 of each 4-week cycle in combination with 3 milligrams per kilogram (3 mg/kg) nivolumab given intravenously (IV), every 2 weeks (Q2W), on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 2) Phase 1b
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Reporting group description:

50 mg Galunisertib administered orally twice daily (BID) on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 3) Phase 1b
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Reporting group description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 4) Phase 1b
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Reporting group description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (NSCLC) Phase 2
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Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (HCC) Phase 2
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Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.
Hepatocellular Carcinoma (HCC)

Reporting group values	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b
Number of subjects	3	5	3
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60.7	47.2	36.0
standard deviation	± 15.6	± 15.8	± 5.3
Gender categorical Units: Subjects			
Female	1	1	1
Male	2	4	2

Race (NIH/OMB)			
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	1	0	0
White	2	5	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
United States	3	3	2
Spain	0	2	1

Reporting group values	Galunisertib + Nivolumab (Cohort 4) Phase 1b	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2
Number of subjects	4	25	1
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	61.5	61.0	64.0
standard deviation	± 9.0	± 8.4	± 0.0
Gender categorical			
Units: Subjects			
Female	3	9	1
Male	1	16	0
Race (NIH/OMB)			
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	1	0	0
White	3	25	1
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
United States	4	1	0
Spain	0	24	1

Reporting group values	Total		
Number of subjects	41		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	16		
Male	25		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	39		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment Units: Subjects			
United States	13		
Spain	28		

End points

End points reporting groups

Reporting group title	Galunisertib + Nivolumab (Cohort 1) Phase 1b
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Reporting group description:

50 milligram (mg) Galunisertib administered orally daily (QD) on Day 1 through Day 14 of each 4-week cycle in combination with 3 milligrams per kilogram (3 mg/kg) nivolumab given intravenously (IV), every 2 weeks (Q2W), on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 2) Phase 1b
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Reporting group description:

50 mg Galunisertib administered orally twice daily (BID) on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 3) Phase 1b
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Reporting group description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 4) Phase 1b
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Reporting group description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (NSCLC) Phase 2
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Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (HCC) Phase 2
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Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.
Hepatocellular Carcinoma (HCC)

Subject analysis set title	Galunisertib + Nivolumab (NSCLC) Phase 2
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Subject analysis set type	Per protocol
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Subject analysis set description:

150 mg Galunisertib given orally twice daily for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV every 2 weeks (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Subject analysis set title	Phase 1b Participants
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Subject analysis set type	Per protocol
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Subject analysis set description:

Cohort 1: 50 mg Galunisertib administered QD on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, every Q2W, on Day 1 and Day 15 for 2 cycles.

Cohort 2: 50 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles.

Cohort 3: 80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles.

Cohort 4: 150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in

combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles.

Subject analysis set title	Galunisertib + Nivolumab (NSCLC + HCC) Phase 2
Subject analysis set type	Per protocol

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Subject analysis set title	Galunisertib + Nivolumab (NSCLC) Phase 2
Subject analysis set type	Per protocol

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Subject analysis set title	Galunisertib + Nivolumab (HCC) Phase 2
Subject analysis set type	Per protocol

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Subject analysis set title	Galunisertib + Nivolumab (NSCLC) Phase 2
Subject analysis set type	Per protocol

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Subject analysis set title	Galunisertib + Nivolumab (HCC) Phase 2
Subject analysis set type	Per protocol

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Primary: Phase 1b: Maximum Tolerated Dose (MTD) of Galunisertib in Combination with Nivolumab

End point title	Phase 1b: Maximum Tolerated Dose (MTD) of Galunisertib in Combination with Nivolumab ^[1]
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End point description:

The MTD is defined as the highest tested dose that has less than 33% probability of causing a dose limiting toxicity (DLT).

Analysis Population Description (APD): All participants who received at least one dose of study drug in Phase 1b per protocol.

End point type	Primary
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End point timeframe:

Cycle 1 through Cycle 2 (Up to 2 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: Per protocol, Maximum Tolerated Dose was assessed during Phase 1b only with all Phase 1b cohorts combined.

End point values	Phase 1b Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: milligrams (mg)				
number (not applicable)	300			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Minimum Concentration (Cmin) of Nivolumab

End point title	Pharmacokinetics (PK): Minimum Concentration (Cmin) of Nivolumab
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End point description:

Minimum Concentration (Cmin) of Nivolumab.

APD: All participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary
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End point timeframe:

PK: Cycle 1 Day 15 Predose; Cycle 2: Day 1: Pre-dose; Day 15: Predose; Cycle 4: Day 1: Predose

End point values	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b	Galunisertib + Nivolumab (Cohort 4) Phase 1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	5	3	4
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (full range (min-max))	33.5 (19.9 to 53.6)	36.2 (11.8 to 58.1)	43.2 (5.45 to 76)	29.2 (9.39 to 63.7)

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	0 ^[2]		
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (full range (min-max))	37.6 (1.08 to 105)	(to)		

Notes:

[2] - Cmin PK data was not available for the HCC cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Area Under the Plasma Concentration -Time Curve of Galunisertib From Time Zero to 24 Hours (AUC [0-24h]) at Steady State

End point title	PK: Area Under the Plasma Concentration -Time Curve of Galunisertib From Time Zero to 24 Hours (AUC [0-24h]) at Steady State
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End point description:

Area under the plasma concentration curve from time zero to 24 hours of galunisertib for Cycle 1 and Cycle 2.

APD: All participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary
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End point timeframe:

PK: Cycle 1 and Cycle 2 Day 1: Predose, 0.5 - 3 hours postdose, Cycle 1 and Cycle 2 Day 14: Predose, 0.5 - 2, 3.5 - 5, and 24 hours postdose through Cycle 4 Day 1 predose

End point values	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b	Galunisertib + Nivolumab (Cohort 4) Phase 1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	4
Units: micrograms*hour per liter ($\mu\text{g}\cdot\text{h}/\text{L}$)				
geometric mean (geometric coefficient of variation)	3060 (\pm 41)	2350 (\pm 46)	2220 (\pm 164)	5580 (\pm 61)

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	1 ^[3]		
Units: micrograms*hour per liter ($\mu\text{g}\cdot\text{h}/\text{L}$)				
geometric mean (geometric coefficient of variation)	7322 (\pm 67)	0 (\pm 0)		

Notes:

[3] - Geometric Mean (CV) could not be calculated for N=1, individual data reported: 6005: $\mu\text{g}\cdot\text{h}/\text{L}$.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Nivolumab Antibodies When Administered in Combination with Galunisertib

End point title	Number of Participants with Anti-Nivolumab Antibodies When Administered in Combination with Galunisertib
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End point description:

Participants with treatment-emergent anti-nivolumab antibodies when administered with galunisertib

were participants with a 4-fold or greater increase in titer from baseline measurement (treatment-boosted). If baseline result is ADA not present, then the subject is TE ADA+, if there is at least 1 postbaseline result of ADA present with titer ≥ 40 (treatment-induced).

APD: All participants who received at least one dose of study drug and were evaluable for TE ADA.

End point type	Secondary
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End point timeframe:

Cycle 1: Days 1, 14, 15 Predose and Day 100 Follow-up; Cycles 2 and 4: Day 1 Predose and Day 100 Follow-up

End point values	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b	Galunisertib + Nivolumab (Cohort 4) Phase 1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	2	3
Units: Count of Participants	0	0	0	0

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	1		
Units: Count of Participants	0	0		

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) ^[4]
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End point description:

PFS was defined as the time from the date of first study treatment to the first evidence of disease progression as defined by response evaluation criteria in solid tumors (RECIST) v1.1 or death from any cause. Progressive Disease (PD) was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. If a participant does not have a complete baseline disease assessment, then the PFS time was censored at the date of randomization, regardless of whether or not objectively determined disease progression or death has been observed for the participant. If a participant was not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time was censored at the last adequate tumor assessment date.

End point type	Secondary
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End point timeframe:

Date of First Study Treatment to Measured Progressive Disease or Death (Up to 35 Months)

APD: All participants who received at least one dose of study drug in the Phase 2 cohorts. Censored participants Galunisertib + Nivolumab (NSCLC) Phase 2 = 6.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol, anti-tumor activity was assessed only on Phase 2 participants.

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	1 ^[5]		
Units: months				
median (confidence interval 95%)	5.26 (1.77 to 9.20)	0 (0 to 0)		

Notes:

[5] - N=1: Median: 5.39, CI: not evaluable (NE)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Percentage of Participants who Achieve Best Overall Tumor Response of Complete Response or Partial Response: Objective Response Rate (ORR)

End point title	Phase 2: Percentage of Participants who Achieve Best Overall Tumor Response of Complete Response or Partial Response: Objective Response Rate (ORR) ^[6]
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End point description:

Objective Response Rate was the percentage of participants achieving a best overall response (BOR) of complete response (CR) or partial response (PR) as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the longest diameters (LD) of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. PD was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more 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.

End point type	Secondary
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End point timeframe:

Baseline to Measured Progressive Disease (Up to 35 Months)

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: Per protocol, anti-tumor activity was assessed only on Phase 2 participants.

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[7]	1 ^[8]		
Units: Percentage of Participants				
number (not applicable)	24.0	0.0		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response (DoR)

End point title Phase 2: Duration of Response (DoR)^[9]

End point description:

Duration of response is measured from the date of documented response to the date of first progression of disease or the date of death due to any cause, whichever is earlier.

APD: All participants who received at least one dose of study drug in Phase 2 cohorts and had a response of complete response or partial response. Censored participants Galunisertib + Nivolumab (NSCLC) Phase 2 = 1.

End point type Secondary

End point timeframe:

Date of Complete Response (CR) or Partial Response (PR) to Date of Objective Disease Progression or Death Due to Any Cause (Up to 35 Months)

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: Per protocol, anti-tumor activity was assessed only on Phase 2 participants.

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	1 ^[10]		
Units: months				
median (full range (min-max))	9.03 (1.97 to 35)	0 (0 to 0)		

Notes:

[10] - There was no response to treatment for the HCC cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Response

End point title Phase 2: Time to Response^[11]

End point description:

Time to response was measured from the date of first study treatment to the first documented response of Complete Response (CR) or Partial Response (PR).

APD: All participants who received at least one dose of study drug in Phase 2 cohorts and had a documented response of CR or PR.

End point type Secondary

End point timeframe:

Date of First Study Treatment to Date of Complete Response or Partial Response (Up to 35 Months)

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: Per protocol, anti-tumor activity was assessed only on Phase 2 participants.

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0 ^[12]		
Units: months				
median (full range (min-max))	4.2 (0.5 to 35)	(to)		

Notes:

[12] - There was no response to treatment for the HCC reporting group.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title | Phase 2: Overall Survival (OS)^[13]

End point description:

Overall Survival is determined from the date of first study treatment until death due to any cause.

APD: All participants who received at least one dose of study drug in Phase 2 cohorts. Censored participants Galunisertib + Nivolumab (NSCLC) Phase 2 = 8.

End point type | Secondary

End point timeframe:

Date of First Study Treatment to Death from Any Cause (Up to 35 Months)

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: Per protocol, anti-tumor activity was assessed only on Phase 2 participants.

End point values	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	1 ^[14]		
Units: months				
median (confidence interval 95%)	11.99 (8.15 to 16.23)	0 (0 to 0)		

Notes:

[14] - N=1 median 14.52 months, CI is non-evaluable.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 34 Months

Adverse event reporting additional description:

All participants who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Galunisertib + Nivolumab (Cohort 1) Phase 1b
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Reporting group description:

50 mg Galunisertib administered orally QD on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV every Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 2) Phase 1b
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Reporting group description:

50 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 3) Phase 1b
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Reporting group description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (Cohort 4) Phase 1b
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Reporting group description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (NSCLC) Phase 2
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Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Reporting group title	Galunisertib + Nivolumab (HCC) Phase 2
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Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Serious adverse events	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 5 (40.00%)	1 / 3 (33.33%)
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) adenocarcinoma of colon alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Vascular disorders angiopathy alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
pericarditis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Nervous system disorders cerebrovascular accident alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
headache alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 5 (20.00%) 0 / 1 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0

noninfective encephalitis alternative dictionary used: MedDRA 23.0 subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (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
General disorders and administration site conditions			
chest pain alternative dictionary used: MedDRA 23.0 subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
dyspepsia alternative dictionary used: MedDRA 23.0 subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
large intestinal obstruction alternative dictionary used: MedDRA 23.0 subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
small intestinal obstruction alternative dictionary used: MedDRA 23.0 subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (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
vomiting alternative dictionary used: MedDRA 23.0 subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

cholelithiasis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Respiratory, thoracic and mediastinal disorders			
chronic obstructive pulmonary disease alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
cough alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 1 / 1 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
dyspnoea alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 1 / 3 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
respiratory failure alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Renal and urinary disorders			
hydronephrosis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	1 / 3 (33.33%) 0 / 1 0 / 0
Musculoskeletal and connective tissue			

disorders			
arthralgia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (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
pain in extremity			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 3 (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
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (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
lower respiratory tract infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (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 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (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
pyelonephritis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory tract infection			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic shock			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (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
urinary tract infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
failure to thrive			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (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

Serious adverse events	Galunisertib + Nivolumab (Cohort 4) Phase 1b	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	13 / 25 (52.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (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
Vascular disorders			
angiopathy			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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
pericarditis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (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
headache			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
noninfective encephalitis			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
dyspepsia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
large intestinal obstruction			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
small intestinal obstruction			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (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
vomiting			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
Hepatobiliary disorders			
cholestasis			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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			
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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
cough			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
dyspnoea			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	2 / 25 (8.00%)	0 / 1 (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
respiratory failure			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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
Renal and urinary disorders			
hydronephrosis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used:			

MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
pain in extremity			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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
lower respiratory tract infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (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 23.0			
subjects affected / exposed	0 / 4 (0.00%)	3 / 25 (12.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyelonephritis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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 tract infection			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 4 (0.00%)	3 / 25 (12.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic shock			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (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
failure to thrive			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Galunisertib + Nivolumab (Cohort 1) Phase 1b	Galunisertib + Nivolumab (Cohort 2) Phase 1b	Galunisertib + Nivolumab (Cohort 3) Phase 1b
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	4 / 5 (80.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

tumour pain alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Vascular disorders hot flush alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
hypertension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
hypotension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
jugular vein thrombosis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
phlebitis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0
General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
chest pain alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
chills			

alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
fatigue			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
influenza like illness			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
malaise			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
oedema peripheral			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
pyrexia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
aphonia			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
bronchial fistula			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
bronchospasm			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
cough			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
dysphonia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
dyspnoea			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
haemoptysis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
oropharyngeal pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

pleural effusion alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
pneumonitis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
productive cough alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
pulmonary embolism alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 5 (40.00%) 2	0 / 3 (0.00%) 0
respiratory acidosis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
rhinitis allergic alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
rhinorrhoea alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Psychiatric disorders depression alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
disorientation alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
insomnia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
amylase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
blood creatinine increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
cd4 lymphocytes decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
cystatin c increased			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
lipase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
lymphocyte count decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
neutrophil count decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
platelet count decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
transaminases increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
troponin t increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
weight decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

white blood cell count decreased alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Injury, poisoning and procedural complications infusion related reaction alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Cardiac disorders cardiac failure alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) mitral valve incompetence alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) pericarditis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) sinus tachycardia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0
Nervous system disorders aura alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) dizziness alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	1 / 5 (20.00%) 1 0 / 5 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0

epilepsy			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
headache			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
hypersomnia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
neurological decompensation			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
neurological symptom			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
neuropathy peripheral			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
paraesthesia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
peripheral motor neuropathy			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
somnolence			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
disseminated intravascular coagulation alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
eosinophilia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders tinnitus alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0
Eye disorders cataract alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
dry eye alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders abdominal distension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
abdominal pain			

alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
cheilitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
constipation			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
diarrhoea			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	2 / 5 (40.00%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
dry mouth			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
dyspepsia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
dysphagia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
flatulence			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
haematemesis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
nausea			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
oesophageal spasm			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
oral pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
rectal haemorrhage			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
stomatitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
vomiting			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 3 (66.67%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	2

Hepatobiliary disorders cholestasis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders dermatitis acneiform alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
dry skin alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
hyperhidrosis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
livedo reticularis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
pruritus alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
rash alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1
rash maculo-papular alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0
skin lesion			

<p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>1 / 5 (20.00%)</p> <p>1</p>	<p>0 / 3 (0.00%)</p> <p>0</p>
<p>Renal and urinary disorders</p> <p>acute kidney injury</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dysuria</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 5 (0.00%)</p> <p>0</p> <p>0 / 5 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>
<p>Endocrine disorders</p> <p>hyperthyroidism</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hypothyroidism</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 5 (0.00%)</p> <p>0</p> <p>1 / 5 (20.00%)</p> <p>1</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>
<p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>arthritis</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>back pain</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>bone pain</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 5 (0.00%)</p> <p>0</p> <p>0 / 5 (0.00%)</p> <p>0</p> <p>0 / 5 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>

alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
flank pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
gouty arthritis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
muscular weakness			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
musculoskeletal chest pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
musculoskeletal pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
myalgia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
neck pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
pain in extremity			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
escherichia infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
gingivitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
influenza			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
otitis externa			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
otitis media			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
pneumonia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
respiratory tract infection			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
rhinitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
skin infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
urinary tract infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
decreased appetite			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
dehydration			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
hypercalcaemia			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hyperglycaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
hyperkalaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hypertriglyceridaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
hypoalbuminaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hypocalcaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hypokalaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hypomagnesaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hypophosphataemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Galunisertib + Nivolumab (Cohort 4) Phase 1b	Galunisertib + Nivolumab (NSCLC) Phase 2	Galunisertib + Nivolumab (HCC) Phase 2
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 4 (100.00%)	23 / 25 (92.00%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) tumour pain alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
Vascular disorders hot flush alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) hypertension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) hypotension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) jugular vein thrombosis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) phlebitis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	2 / 25 (8.00%) 5 0 / 25 (0.00%) 0 3 / 25 (12.00%) 4 1 / 25 (4.00%) 1 0 / 25 (0.00%) 0	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0
General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 4 (0.00%)	4 / 25 (16.00%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
chest pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
chills			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
fatigue			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	6 / 25 (24.00%)	0 / 1 (0.00%)
occurrences (all)	2	10	0
influenza like illness			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
malaise			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
oedema peripheral			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

pyrexia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	5 / 25 (20.00%) 8	0 / 1 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
aphonia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
bronchial fistula alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
bronchospasm alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
chronic obstructive pulmonary disease alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
cough alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	3 / 25 (12.00%) 4	0 / 1 (0.00%) 0
dysphonia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
dyspnoea alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 25 (8.00%) 2	0 / 1 (0.00%) 0
haemoptysis			

alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
oropharyngeal pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
pleural effusion			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
pneumonitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
productive cough			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
pulmonary embolism			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
respiratory acidosis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
rhinitis allergic			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
rhinorrhoea			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 25 (0.00%) 0	1 / 1 (100.00%) 1
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 25 (0.00%) 0	0 / 1 (0.00%) 0
disorientation			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 25 (0.00%) 0	0 / 1 (0.00%) 0
insomnia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 3	2 / 25 (8.00%) 4	0 / 1 (0.00%) 0
amylase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	3 / 4 (75.00%) 6	2 / 25 (8.00%) 2	0 / 1 (0.00%) 0
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 4	2 / 25 (8.00%) 4	0 / 1 (0.00%) 0
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 4	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
blood creatinine increased			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
cd4 lymphocytes decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
cystatin c increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	4	2	0
lipase increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	7	1	0
lymphocyte count decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
neutrophil count decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
platelet count decreased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	3 / 25 (12.00%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
transaminases increased			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0

troponin t increased alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
weight decreased alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 2	0 / 1 (0.00%) 0
white blood cell count decreased alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 3	0 / 25 (0.00%) 0	0 / 1 (0.00%) 0
Injury, poisoning and procedural complications infusion related reaction alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
Cardiac disorders cardiac failure alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
mitral valve incompetence alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
pericarditis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
sinus tachycardia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	0 / 25 (0.00%) 0	0 / 1 (0.00%) 0
Nervous system disorders			

aura			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
dizziness			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	3 / 25 (12.00%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
epilepsy			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
headache			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	5 / 25 (20.00%)	0 / 1 (0.00%)
occurrences (all)	1	6	0
hypersomnia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
neurological decompensation			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
neurological symptom			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
neuropathy peripheral			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
paraesthesia			
alternative dictionary used: MedDRA 23.0			

<p>subjects affected / exposed occurrences (all)</p> <p>peripheral motor neuropathy alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p> <p>somnolence alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p>	<p>0 / 4 (0.00%) 0</p> <p>0 / 4 (0.00%) 0</p> <p>0 / 4 (0.00%) 0</p>	<p>1 / 25 (4.00%) 1</p> <p>2 / 25 (8.00%) 2</p> <p>0 / 25 (0.00%) 0</p>	<p>0 / 1 (0.00%) 0</p> <p>0 / 1 (0.00%) 0</p> <p>0 / 1 (0.00%) 0</p>
<p>Blood and lymphatic system disorders</p> <p>anaemia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p> <p>disseminated intravascular coagulation alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p> <p>eosinophilia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p>	<p>1 / 4 (25.00%) 3</p> <p>0 / 4 (0.00%) 0</p> <p>0 / 4 (0.00%) 0</p>	<p>3 / 25 (12.00%) 3</p> <p>1 / 25 (4.00%) 1</p> <p>1 / 25 (4.00%) 2</p>	<p>0 / 1 (0.00%) 0</p> <p>0 / 1 (0.00%) 0</p> <p>0 / 1 (0.00%) 0</p>
<p>Ear and labyrinth disorders</p> <p>tinnitus alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p>	<p>0 / 4 (0.00%) 0</p>	<p>0 / 25 (0.00%) 0</p>	<p>0 / 1 (0.00%) 0</p>
<p>Eye disorders</p> <p>cataract alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)</p> <p>dry eye alternative dictionary used: MedDRA 23.0</p>	<p>0 / 4 (0.00%) 0</p>	<p>1 / 25 (4.00%) 1</p>	<p>0 / 1 (0.00%) 0</p>

subjects affected / exposed	0 / 4 (0.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	3 / 25 (12.00%)	0 / 1 (0.00%)
occurrences (all)	0	6	0
abdominal pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
cheilitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
constipation			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	4 / 25 (16.00%)	0 / 1 (0.00%)
occurrences (all)	1	5	0
diarrhoea			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	7 / 25 (28.00%)	0 / 1 (0.00%)
occurrences (all)	1	10	0
dry mouth			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	4 / 25 (16.00%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
dyspepsia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
dysphagia			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
flatulence			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
haematemesis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
nausea			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	6 / 25 (24.00%)	0 / 1 (0.00%)
occurrences (all)	2	6	0
oesophageal spasm			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
oral pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
rectal haemorrhage			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

stomatitis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	3 / 25 (12.00%) 4	0 / 1 (0.00%) 0
vomiting alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	3 / 25 (12.00%) 3	0 / 1 (0.00%) 0
Hepatobiliary disorders cholestasis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 25 (8.00%) 2	0 / 1 (0.00%) 0
Skin and subcutaneous tissue disorders dermatitis acneiform alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 3	0 / 1 (0.00%) 0
dry skin alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	3 / 25 (12.00%) 3	0 / 1 (0.00%) 0
hyperhidrosis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
livedo reticularis alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
pruritus alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	9 / 25 (36.00%) 14	0 / 1 (0.00%) 0
rash			

<p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 4 (25.00%)</p> <p>1</p>	<p>2 / 25 (8.00%)</p> <p>4</p>	<p>0 / 1 (0.00%)</p> <p>0</p>
<p>rash maculo-papular</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 4 (50.00%)</p> <p>2</p>	<p>5 / 25 (20.00%)</p> <p>10</p>	<p>0 / 1 (0.00%)</p> <p>0</p>
<p>skin lesion</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p>	<p>0 / 25 (0.00%)</p> <p>0</p>	<p>0 / 1 (0.00%)</p> <p>0</p>
<p>Renal and urinary disorders</p> <p>acute kidney injury</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dysuria</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	<p>1 / 25 (4.00%)</p> <p>1</p> <p>1 / 25 (4.00%)</p> <p>1</p>	<p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p>
<p>Endocrine disorders</p> <p>hyperthyroidism</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hypothyroidism</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	<p>1 / 25 (4.00%)</p> <p>1</p> <p>4 / 25 (16.00%)</p> <p>4</p>	<p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p>
<p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>arthritis</p>	<p>0 / 4 (0.00%)</p> <p>0</p>	<p>2 / 25 (8.00%)</p> <p>3</p>	<p>0 / 1 (0.00%)</p> <p>0</p>

alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	8	0
back pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	6 / 25 (24.00%)	0 / 1 (0.00%)
occurrences (all)	0	6	0
bone pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
flank pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
gouty arthritis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
muscular weakness			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
musculoskeletal chest pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
musculoskeletal pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
myalgia			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
neck pain			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
pain in extremity			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	4 / 25 (16.00%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
escherichia infection			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
gingivitis			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
influenza			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
otitis externa			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
otitis media			
alternative dictionary used: MedDRA 23.0			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
pneumonia alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 25 (0.00%) 0	0 / 1 (0.00%) 0
respiratory tract infection alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	4 / 25 (16.00%) 4	0 / 1 (0.00%) 0
rhinitis alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
skin infection alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 25 (8.00%) 2	0 / 1 (0.00%) 0
upper respiratory tract infection alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	4 / 25 (16.00%) 4	0 / 1 (0.00%) 0
urinary tract infection alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	2 / 25 (8.00%) 4	0 / 1 (0.00%) 0
Metabolism and nutrition disorders			
cachexia alternative dictionary used: MedDRA 23.0			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 25 (4.00%) 1	0 / 1 (0.00%) 0
decreased appetite alternative dictionary used: MedDRA 23.0			

subjects affected / exposed	1 / 4 (25.00%)	7 / 25 (28.00%)	0 / 1 (0.00%)
occurrences (all)	1	11	0
dehydration			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
hypercalcaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	1 / 25 (4.00%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
hyperglycaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	3 / 25 (12.00%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
hyperkalaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
hypertriglyceridaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	0 / 4 (0.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
hypoalbuminaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
hypocalcaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	0 / 25 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
hypokalaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 4 (50.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	2	2	0

hypomagnesaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
hypophosphataemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	1 / 4 (25.00%)	2 / 25 (8.00%)	0 / 1 (0.00%)
occurrences (all)	1	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2015	Amendment A: <ul style="list-style-type: none">• Addition of 2 cohorts• Addition of study ECG's• Addition of \geq CTCAE Grade 3 thrombocytopenia• Addition of serum pregnancy test on Day 1 of every cycle• Added ECHO at the 30-day follow-up visit• Additional patient enrolled predose level to allow for unforeseen discontinuation
30 August 2016	Amendment B: Removed high-sensitivity C-reactive protein
31 January 2017	Amendment C: Removal of glioblastoma cohort <ul style="list-style-type: none">• Requirement for ECHO at the 30-day follow-up visit added back in protocol (c)• Add hepatitis B surface antigen testing back in protocol (c)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due low enrollment, the HCC cohort was terminated early.

Notes: