Clinical trial results:
A Phase 2 Study of LY2157299 Monohydrate Monotherapy or LY2157299 Monohydrate Plus Lomustine Therapy Compared to Lomustine Monotherapy in Patients With Recurrent Glioblastoma

Summary

EudraCT number	2011-004418-40
Trial protocol	ES DE BE IT PL NL
Global end of trial date	10 October 2024

Results information

Result version number	v2 (current)
This version publication date	18 January 2026
First version publication date	24 October 2025
Version creation reason	• New data added to full data set New Data updated

Trial information

Trial identification

Sponsor protocol code	H9H-MC-JBAL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01582269
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 13849

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, 1 877-CTLilly, EU_Lilly_Clinical_Trials@lilly.com
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559, EU_Lilly_Clinical_Trials@lilly.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to see whether treatment with LY2157299 on its own, LY2157299 plus lomustine therapy or lomustine plus placebo can help participants with brain cancer

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Australia: 20
Worldwide total number of subjects	158
EEA total number of subjects	113

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)	122
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All the treated participants who experienced progressive disease or died were considered study completers, while those who withdrew consent or were lost to follow-up were not.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Galunisertib

Arm description:

Participants received Galunisertib 300 milligrams (mg) orally twice daily (BID) for 14 days, followed by 14 days of rest in a 28-day cycle.
Treatment continued until disease progression or discontinuation criteria were met.

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

Dosage and administration details:

Participants received Galunisertib 300 milligrams (mg) orally twice daily (BID) for 14 days, followed by 14 days of rest in a 28-day cycle.

Arm title	Arm B: Galunisertib + Lomustine

Arm description:

Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Participants received a first dose of Lomustine at 100 milligrams per square meter (mg/m²) administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.
Treatment continued until disease progression or discontinuation criteria were met.

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

Dosage and administration details:

Participants received Galunisertib 300 milligrams (mg) orally twice daily (BID) for 14 days, followed by 14 days of rest in a 28-day cycle.

Investigational medicinal product name	Lomustine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of Lomustine at 100 milligrams per square meter (mg/m²) administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.

Arm title	Arm C: Lomustine + Placebo

Arm description:

Participants received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.
Participants received Galunisertib-matched Placebo orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Treatment continued until disease progression or discontinuation criteria were met.

Arm type	Active comparator
Investigational medicinal product name	Lomustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Galunisertib-matched Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Galunisertib-matched Placebo orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.

Number of subjects in period 1	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo
Started	39	79	40
Received at Least One Dose of Study Drug	39	79	40
Safety Analysis Population	39	78	40
Completed	38	79	40
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Galunisertib
Reporting group description:	
Participants received Galunisertib 300 milligrams (mg) orally twice daily (BID) for 14 days, followed by 14 days of rest in a 28-day cycle. Treatment continued until disease progression or discontinuation criteria were met.	
Reporting group title	Arm B: Galunisertib + Lomustine
Reporting group description:	
Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle. Participants received a first dose of Lomustine at 100 milligrams per square meter (mg/m²) administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator. Treatment continued until disease progression or discontinuation criteria were met.	
Reporting group title	Arm C: Lomustine + Placebo
Reporting group description:	
Participants received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator. Participants received Galunisertib-matched Placebo orally BID for 14 days, followed by 14 days of rest in a 28-day cycle. Treatment continued until disease progression or discontinuation criteria were met.	

Reporting group values	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo
Number of subjects	39	79	40
Age categorical			
Analysis Population Description (APD): All randomized participants.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	30	61	31
From 65-84 years	9	18	9
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	18	21	17
Male	21	58	23
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	6	2
Not Hispanic or Latino	29	56	27
Unknown or Not Reported	7	17	11
Race (NIH/OMB) Units: Subjects			

Asian	2	1	1
Black or African American	0	2	0
White	30	60	29
Unknown or Not Reported	7	16	10
Region of Enrollment Units: Subjects			
Canada	0	3	1
Belgium	3	8	3
United States	7	8	6
Poland	1	1	0
Italy	8	14	8
Australia	4	14	2
France	7	17	11
Germany	4	7	5
Spain	5	6	3
Netherlands	0	1	1

Reporting group values	Total		
Number of subjects	158		
Age categorical			
Analysis Population Description (APD): All randomized participants.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	122		
From 65-84 years	36		
85 years and over	0		
Gender categorical Units: Subjects			
Female	56		
Male	102		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11		
Not Hispanic or Latino	112		
Unknown or Not Reported	35		
Race (NIH/OMB) Units: Subjects			
Asian	4		
Black or African American	2		
White	119		
Unknown or Not Reported	33		
Region of Enrollment Units: Subjects			
Canada	4		
Belgium	14		

United States	21		
Poland	2		
Italy	30		
Australia	20		
France	35		
Germany	16		
Spain	14		
Netherlands	2		

End points

End points reporting groups

Reporting group title	Arm A: Galunisertib

Reporting group description:

Participants received Galunisertib 300 milligrams (mg) orally twice daily (BID) for 14 days, followed by 14 days of rest in a 28-day cycle.
Treatment continued until disease progression or discontinuation criteria were met.

Reporting group title	Arm B: Galunisertib + Lomustine

Reporting group description:

Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Participants received a first dose of Lomustine at 100 milligrams per square meter (mg/m²) administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.
Treatment continued until disease progression or discontinuation criteria were met.

Reporting group title	Arm C: Lomustine + Placebo

Reporting group description:

Participants received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.
Participants received Galunisertib-matched Placebo orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Treatment continued until disease progression or discontinuation criteria were met.

Subject analysis set title	Arm A: Galunisertib and Arm B: Galunisertib + Lomustine
Subject analysis set type	Per protocol

Subject analysis set description:

Arm A: Galunisertib: Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle until disease progression, death, or discontinuation criteria were met.
Arm B: Galunisertib + Lomustine: Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle, plus received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator, until disease progression, death, or discontinuation criteria were met.

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from the date of randomization until death from any cause. For participants not known to have died by the data-inclusion cutoff date, OS is censored at the last date they were known to be alive. APD:All randomized participants who received at least one dose of study drug (including the censored participants). Number of participants censored in Arm A: Galunisertib = 9; Arm B: Galunisertib + Lomustine = 8; and Arm C: Lomustine + Placebo = 6.

End point type	Primary

End point timeframe:

Randomization to Date of Death from Any Cause (Up To 20.5 Months)

End point values	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39[1]	79[2]	40[3]	
Units: Months				
median (confidence interval 95%)	8.0 (5.7 to	6.7 (5.3 to 8.5)	7.5 (5.6 to	

	11.7)	10.3)

Notes:

[1] - Data reported is median with 95% credible interval.

[2] - Data reported is median with 95% credible interval.

[3] - Data reported is median with 95% credible interval.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The Bayesian analyses below include credible intervals rather than confidence intervals for the hazard ratios.The posterior probability treatment difference is 0.6158.

Comparison groups	Arm A: Galunisertib v Arm C: Lomustine + Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
Method	Bayesian exponential-likelihood model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9336
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.49

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The Bayesian analyses below include credible intervals rather than confidence intervals for the hazard ratios.The posterior probability treatment difference is 0.2628.

Comparison groups	Arm B: Galunisertib + Lomustine v Arm C: Lomustine + Placebo
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
Method	Bayesian exponential-likelihood model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.65

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the time from randomization to the date of the first observation of objective disease

progression or death from any cause, whichever occurred first. Participants known to be alive and without disease progression were censored at the date of their last objective progression-free disease assessment prior to the initiation of any subsequent systemic anticancer therapy. APD:All randomized participants who received at least one dose of study drug (including the censored participants). Number of participants censored in Arm A: Galunisertib = 7; Arm B: Galunisertib + Lomustine = 8; and Arm C: Lomustine + Placebo = 4.

End point type	Secondary

End point timeframe:

Randomization to Objective Progression or Death Due to Any Cause (Up To 19 Months)

End point values	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	79	40	
Units: Months				
median (confidence interval 95%)	1.8 (1.6 to 3.0)	1.8 (1.7 to 1.8)	1.9 (1.7 to 1.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Tumour Response

End point title	Percentage of Participants With Tumour Response

End point description:

Tumour response was assessed using Response Assessment in Neuro-Oncology (RANO) criteria. Responses included Complete Response (CR),Partial Response (PR), Stable Disease (SD),and Progressive Disease (PD). CR required disappearance of all enhancing lesions, no new lesions, stable or improved non-enhancing lesions, and no corticosteroid use.PR was defined as ≥50% reduction in enhancing lesion size, no new lesions, stable or improved non-enhancing lesions,and stable or reduced corticosteroid use.SD indicated no significant change in lesion size or clinical status. PD was defined as ≥25% increase in lesion size, new lesions, or clinical deterioration. Percentage of participants with tumor response is defined as the percentage of participants who achieved these tumor responses based on RANO criteria.Participants whose tumor response could not be assessed due to inadequate imaging data were categorized as 'Unknown'. APD:All randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Randomization until measured progressive disease (Up To 19 Months)

End point values	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	79	40	
Units: Percentage of participants				
number (not applicable)				
CR	0.0	1.3	0.0	
PR	5.1	0.0	0.0	

SD	25.6	20.3	30.0	
PD	53.8	63.3	65.0	
Unknown	15.4	15.2	5.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics (PopPK): Absorption Rate Constant of Galunisertib (Arm A: Galunisertib and Arm B: Galunisertib + Lomustine)

End point title	Population Pharmacokinetics (PopPK): Absorption Rate Constant of Galunisertib (Arm A: Galunisertib and Arm B: Galunisertib + Lomustine)

End point description:

The absorption rate constant (Ka) of Galunisertib was estimated using PopPK modeling based on plasma concentration-time data collected during Cycle 1. A two-compartment model with first-order absorption was applied using nonlinear mixed-effects modeling. Samples were collected at the following time points: Cycle 1 Day 1: Predose, 0.5-2 hours (h), 3.5-5 h, and 48 h post-dose; Day 14: Predose, 0.5-2 h, 3.5-5 h, 24 h, and 48 h post last dose. Individual participant Ka values were derived from model-estimated parameters using all available PK timepoints.The reported outcome is the mean of these individual Ka estimates across both treatment arms (Arm A: Galunisertib; Arm B: Galunisertib + Lomustine). APD:All randomized participants who received ≥1 dose of Galunisertib (Arm A and Arm B) and had evaluable PK data were included in the analysis. As prespecified in the statistical analysis plan, PK analyses of Galunisertib exposure parameters were conducted using data combined from both arms.

End point type	Secondary

End point timeframe:

Cycle (C) 1: Day (D)1: Predose, 0.5–2 hours (h), 3.5–5 h, and 48 h post-dose; Day 14: Predose, 0.5–2 h, 3.5–5 h, 24 h, and 48 h post last dose

End point values	Arm A: Galunisertib and Arm B: Galunisertib + Lomustine			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: One per hour (1/hour)				
arithmetic mean (standard error)	2.28 (± 26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics (PopPK): Mean Steady State Apparent Volume of Distribution (Vss) of Galunisertib (Arm A: Galunisertib and Arm B: Galunisertib + Lomustine)

End point title	Population Pharmacokinetics (PopPK): Mean Steady State Apparent Volume of Distribution (Vss) of Galunisertib (Arm A: Galunisertib and Arm B: Galunisertib + Lomustine)

End point description:

The Vss at steady state of Galunisertib was estimated using PopPK modeling based on plasma concentration-time data collected during Cycle 1.A two-compartment model was applied using nonlinear mixed-effects modeling. Samples were collected at the following time points: Cycle 1 Day 1: Predose, 0.5-2 hours (h), 3.5-5 h, and 48 h post-dose; Day 14: Predose, 0.5-2 h, 3.5-5 h, 24 h, and 48 h post last dose. Individual participant Vss values were derived from model-estimated parameters using all available PK timepoints. The reported outcome is the mean of individual Vss estimates across both treatment arms (Arm A: Galunisertib; Arm B: Galunisertib + Lomustine). APD:All randomized participants who received ≥1 dose of Galunisertib (Arm A and Arm B) and had evaluable PK data were included in the analysis. As prespecified in the statistical analysis plan, PK analyses of Galunisertib exposure parameters were conducted using data combined from both arms.

End point type	Secondary

End point timeframe:

Cycle (C) 1: Day (D)1: Predose, 0.5–2 hours (h), 3.5–5 h, and 48 h post-dose; Day 14: Predose, 0.5–2 h, 3.5–5 h, 24 h, and 48 h post last dose

End point values	Arm A: Galunisertib and Arm B: Galunisertib + Lomustine			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: Liters (L)				
arithmetic mean (standard error)	175 (± 8.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics (PopPK): Mean Population Clearance of Galunisertib (Arm A: Galunisertib and Arm B: Galunisertib + Lomustine)

End point title	Population Pharmacokinetics (PopPK): Mean Population Clearance of Galunisertib (Arm A: Galunisertib and Arm B: Galunisertib + Lomustine)

End point description:

The apparent clearance (CL/F) of Galunisertib was estimated using PopPK modeling based on plasma concentration-time data collected during Cycle 1. A two-compartment model was applied using nonlinear mixed-effects modeling. Samples were collected at the following time points: Cycle 1 Day 1: Predose, 0.5-2 hours (h), 3.5-5 h, and 48 h post-dose; Day 14: Predose, 0.5-2 h, 3.5-5 h, 24 h, and 48 h post last dose. Individual participant CL/F values were derived from model-estimated parameters using all available PK timepoints. The reported outcome is the mean of these individual CL/F estimates across both treatment arms (Arm A: Galunisertib; Arm B: Galunisertib + Lomustine). APD: All randomized participants who received ≥1 dose of Galunisertib (Arm A and Arm B) and had evaluable PK data were included in the analysis. As prespecified in the statistical analysis plan, PK analyses of Galunisertib exposure parameters were conducted using data combined from both arms.

End point type	Secondary

End point timeframe:

Cycle (C) 1: Day (D)1: Predose, 0.5–2 hours (h), 3.5–5 h, and 48 h post-dose; Day 14: Predose, 0.5–2 h, 3.5–5 h, 24 h, and 48 h post last dose

End point values	Arm A: Galunisertib and Arm B: Galunisertib + Lomustine			
Subject group type	Subject analysis set			
Number of subjects analysed	114			
Units: Liter per hour (L/hr)				
arithmetic mean (standard error)	37.5 (± 5.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Neurocognitive Function Using Hopkins Verbal Learning Test-Revised (HVLT-R)

End point title	Change From Baseline in Neurocognitive Function Using Hopkins Verbal Learning Test-Revised (HVLT-R)

End point description:

The Hopkins Verbal Learning Test-Revised comprises:
- 3 Learning Trials: Participants were presented with a list of 12 words (from 3 semantic categories) and were asked to recall them to test verbal learning and memory.
- Delayed Recall Trial: Conducted 20-25 minutes after the 3rd learning trial to test memory retention.
- Delayed Recognition Trial: Participants identified previously presented words from a list that included 12 distractors to test recognition discrimination.
Scoring Components:
- Total Recall Score (0-36): Sum of correctly recalled words across the 3 learning trials.
- Delayed Recall Score (0-12): Number of correct words recalled after the delay.
- Recognition Discrimination Index Score (+12 to -12): Calculated as the number of true positives (correctly identified words) minus false positives (incorrectly identified words, i.e., distractors).
For each of the 3 reported scores, higher scores = better neurocognitive performance; lower scores = decline.

End point type	Secondary

End point timeframe:

Baseline, Month 20 (APD: All randomized participants who received ≥1 dose and had baseline and ≥1 post-baseline measurement for this outcome).

End point values	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36[4]	74[5]	39	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Total Recall Score	-0.2 (± 1.4)	-0.2 (± 1.2)	-0.3 (± 1.5)	
Delayed Recall Score	-0.8 (± 2.2)	0.0 (± 1.4)	0.1 (± 1.3)	
Recognition Discrimination Index Score	-1.3 (± 5.1)	0.7 (± 4.1)	0.1 (± 2.0)	

Notes:

[4] - For Delayed Recall Score and Recognition Discrimination Index Score Number Analyzed(n) =35

[5] - For Delayed Recall Score and Recognition Discrimination Index Score n =71

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MD Anderson Symptom Inventory Brain Tumor (MDASI-BT) Symptom and Interference Severity Scores: (Brain Tumor Symptoms, Core Symptoms, Interference Symptoms)

End point title	Change From Baseline in MD Anderson Symptom Inventory Brain Tumor (MDASI-BT) Symptom and Interference Severity Scores: (Brain Tumor Symptoms, Core Symptoms, Interference Symptoms)

End point description:

The MDASI-BT assesses the severity of multiple brain tumor-related symptoms and the impact of these symptoms on daily functioning in the last 24 hours. It includes:
13 core symptoms measuring severity of pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, memory problems, lack of appetite, drowsiness, dry mouth, sadness, vomiting, and numbness/tingling, rated 0-10, where 0 = "not present" and 10 = "as bad as you can imagine."
9 brain tumor-specific symptoms assess severity of difficulty speaking, weakness, seizures, difficulty understanding, vision changes, appearance changes, bowel pattern changes, concentration problems, and irritability, rated 0-10, where 0 = "not present" and 10 = "as bad as you can imagine."
6 interference items assess impact on general activity, mood, work, relations, walking, and enjoyment of life, rated 0-10, where 0 = "did not interfere" and 10 = "interfered completely."

End point type	Secondary

End point timeframe:

Baseline, Month 21 (APD: All randomized participants who received ≥1 dose and had baseline and ≥1 post-baseline measurement for this outcome).

End point values	Arm A: Galunisertib	Arm B: Galunisertib + Lomustine	Arm C: Lomustine + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38[6]	77	38	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Brain Tumor Symptoms	0.0 (± 2.3)	0.3 (± 1.9)	-0.3 (± 1.9)	
Core Symptoms	0.0 (± 1.5)	0.3 (± 1.5)	0.3 (± 0.9)	
Interference Symptoms	0.2 (± 2.8)	0.8 (± 2.2)	1.1 (± 3.0)	

Notes:

[6] - For Interference Symptoms n=37

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up to 11 years 4 months

Adverse event reporting additional description:

Safety Analysis Population includes all randomized participants who received ≥1 dose of study drug, analyzed by actual treatment received. 1 participant in Arm B received only Galunisertib (no Lomustine) Thus, Arm A = 40 and Arm B=78. 1 participant in Arm C received only placebo thus Arm C: Lomustine + Placebo = 39; Arm C: Placebo Alone = 1.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Arm A: Galunisertib and Arm B: Galunisertib (Monotherapy)

Reporting group description:

Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Treatment continued until disease progression, death, or discontinuation criteria were met.

Reporting group title	Arm C: Lomustine + Placebo (Placebo Alone)

Reporting group description:

Participants randomized to Arm C who did not receive the planned treatment but received Galunisertib-matched placebo alone were categorized under this group.

Reporting group title	Arm C: Lomustine + Placebo

Reporting group description:

Participants received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.
Participants received Galunisertib-matched Placebo orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Treatment continued until disease progression, death, or discontinuation criteria were met.

Reporting group title	Arm B: Galunisertib + Lomustine

Reporting group description:

Participants received Galunisertib 300 mg orally BID for 14 days, followed by 14 days of rest in a 28-day cycle.
Participants received a first dose of Lomustine at 100 mg/m² administered orally. Thereafter, starting with the second dose, Lomustine was administered orally once every 6 weeks at 100-130 mg/m², at the discretion of the investigator.
Treatment continued until disease progression, death, or discontinuation criteria were met.

Serious adverse events	Arm A: Galunisertib and Arm B: Galunisertib (Monotherapy)	Arm C: Lomustine + Placebo (Placebo Alone)	Arm C: Lomustine + Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 40 (52.50%)	1 / 1 (100.00%)	15 / 39 (38.46%)
number of deaths (all causes)	37	1	38
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

malignant neoplasm progression			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tumour haemorrhage			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertension			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypotension			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
phlebitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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			
asthenia			

alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
fatigue			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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 physical health deterioration			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
oedema peripheral			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
Immune system disorders			
hypersensitivity			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
Respiratory, thoracic and mediastinal disorders			
lung disorder			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
pulmonary embolism			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
pulmonary oedema			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
delirium			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
hallucination			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
insomnia			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
mania			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mental status changes			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
psychotic disorder due to a general medical condition			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
eastern cooperative oncology group performance status worsened			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
electrocardiogram repolarisation abnormality			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
neutrophil count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
white blood cell count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
hip fracture			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
meningitis chemical			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
aphasia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
ataxia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
brain oedema			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (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
cerebral haemorrhage			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
depressed level of consciousness			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
facial paresis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
headache			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hemiparesis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hydrocephalus			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
iiird nerve disorder			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
intracranial pressure increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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

neurological decompensation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
non-24-hour sleep-wake disorder			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
partial seizures			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
post herpetic neuralgia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
seizure			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	7 / 40 (17.50%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
somnolence			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
status epilepticus			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
subdural hygroma			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
Blood and lymphatic system disorders			
febrile neutropenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutropenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
pancytopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	1 / 1 (100.00%)	0 / 39 (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
dysphagia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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 intestine perforation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
nausea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
urinary retention			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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			
muscular weakness			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
cellulitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
clostridium colitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
herpes zoster			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (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
peritonitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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 27.1			

subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
varicella zoster virus infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (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
hyperglycaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm B: Galunisertib + Lomustine		
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 78 (39.74%)		
number of deaths (all causes)	75		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
malignant neoplasm progression			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
tumour haemorrhage				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
deep vein thrombosis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hypertension				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypotension				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
phlebitis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
asthenia				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
fatigue				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	2 / 78 (2.56%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
general physical health deterioration				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
multiple organ dysfunction syndrome				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
oedema peripheral				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
hypersensitivity				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
lung disorder				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pulmonary embolism				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pulmonary oedema				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
agitation				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
delirium				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hallucination				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
insomnia				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
mania				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
mental status changes				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
psychotic disorder due to a general medical condition				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
alanine aminotransferase increased				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	2 / 78 (2.56%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
aspartate aminotransferase increased				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
eastern cooperative oncology group performance status worsened				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
electrocardiogram repolarisation abnormality				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
gamma-glutamyltransferase increased				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
neutrophil count decreased				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
white blood cell count decreased				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
fall				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hip fracture				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
meningitis chemical				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
aphasia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ataxia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
brain oedema				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	5 / 78 (6.41%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
cerebral haemorrhage				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
depressed level of consciousness				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
facial paresis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
headache			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
hemiparesis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
hydrocephalus			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
iiird nerve disorder			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
intracranial pressure increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

neurological decompensation				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
non-24-hour sleep-wake disorder				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
partial seizures				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
post herpetic neuralgia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
seizure				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	4 / 78 (5.13%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
somnolence				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
status epilepticus				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
subdural hygroma				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
syncope				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
febrile neutropenia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
neutropenia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pancytopenia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
diarrhoea				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	0 / 78 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
dysphagia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
large intestine perforation				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
nausea				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
vomiting				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
urinary retention				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
muscular weakness				
alternative dictionary used: MedDRA 27.1				

subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
cellulitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
clostridium colitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
herpes zoster			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
peritonitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
pneumonia			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
sepsis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
varicella zoster virus infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hyperglycaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A: Galunisertib and Arm B: Galunisertib (Monotherapy)	Arm C: Lomustine + Placebo (Placebo Alone)	Arm C: Lomustine + Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 40 (85.00%)	0 / 1 (0.00%)	31 / 39 (79.49%)
General disorders and administration site conditions			

asthenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
fatigue			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	10 / 40 (25.00%)	0 / 1 (0.00%)	14 / 39 (35.90%)
occurrences (all)	10	0	15
oedema peripheral			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 40 (7.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	3	0	2
pyrexia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	1	0	3
Reproductive system and breast disorders			
vaginal haemorrhage			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[1]	1 / 19 (5.26%)	0 / 1 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
dyspnoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	2	0	2
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
anxiety			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	2	0	2
confusional state			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 40 (7.50%)	0 / 1 (0.00%)	5 / 39 (12.82%)
occurrences (all)	3	0	5
depression			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 40 (7.50%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	3	0	1
insomnia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	2	0	2
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	2	0	3
neutrophil count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	4
platelet count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	4 / 39 (10.26%)
occurrences (all)	1	0	4
weight decreased			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
weight increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	5 / 39 (12.82%)
occurrences (all)	1	0	5
white blood cell count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	4 / 39 (10.26%)
occurrences (all)	0	0	4
Cardiac disorders			
pericardial effusion			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
amnesia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
aphasia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	6 / 40 (15.00%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	7	0	3
ataxia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
dizziness			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
headache			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	11 / 40 (27.50%)	0 / 1 (0.00%)	10 / 39 (25.64%)
occurrences (all)	12	0	13
hemiparesis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	6 / 39 (15.38%)
occurrences (all)	0	0	6
hypoaesthesia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	3	0	0
nervous system disorder			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
paraesthesia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	4 / 39 (10.26%)
occurrences (all)	1	0	4
seizure			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	4 / 39 (10.26%)
occurrences (all)	2	0	6
somnolence			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
tremor			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 40 (7.50%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	3	0	1
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	4 / 39 (10.26%)
occurrences (all)	1	0	5
lymphopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	4 / 39 (10.26%)
occurrences (all)	2	0	4
neutropenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
thrombocytopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	12 / 39 (30.77%)
occurrences (all)	4	0	12
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 40 (7.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	3	0	0
abdominal pain upper			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
constipation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	2	0	4
diarrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 40 (10.00%)	0 / 1 (0.00%)	6 / 39 (15.38%)
occurrences (all)	7	0	7
haemorrhoids			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
nausea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	6 / 40 (15.00%)	0 / 1 (0.00%)	8 / 39 (20.51%)
occurrences (all)	6	0	10
stomatitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
vomiting			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 40 (10.00%)	0 / 1 (0.00%)	8 / 39 (20.51%)
occurrences (all)	4	0	11
Skin and subcutaneous tissue disorders			
dry skin			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
hirsutism			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[2]	1 / 19 (5.26%)	0 / 1 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
pruritus			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 40 (12.50%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	5	0	0
Renal and urinary disorders			
urinary incontinence			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 40 (10.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	4	0	0
Endocrine disorders			
cushingoid			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	2	0	3
back pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
muscular weakness			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 40 (2.50%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
myalgia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
neck pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
pain in extremity			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 40 (7.50%)	0 / 1 (0.00%)	3 / 39 (7.69%)
occurrences (all)	4	0	3
Infections and infestations			
urinary tract infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 40 (5.00%)	0 / 1 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
Metabolism and nutrition disorders			

hyperglycaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 40 (0.00%)	0 / 1 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Arm B: Galunisertib + Lomustine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 78 (88.46%)		
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
fatigue			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	20 / 78 (25.64%)		
occurrences (all)	25		
oedema peripheral			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
pyrexia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	6		
Reproductive system and breast disorders			
vaginal haemorrhage			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[1]	0 / 20 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	11		
dyspnoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	7		
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	3		
anxiety			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	7		
confusional state			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	5		
depression			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	4		
insomnia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	7		
neutrophil count decreased			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	12		
platelet count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	5		
weight decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	9		
weight increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	3		
white blood cell count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	13		
Cardiac disorders			
pericardial effusion			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
Nervous system disorders			
amnesia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
aphasia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
ataxia			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	4 / 78 (5.13%)			
occurrences (all)	4			
dizziness				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	8 / 78 (10.26%)			
occurrences (all)	9			
headache				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	20 / 78 (25.64%)			
occurrences (all)	27			
hemiparesis				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	7 / 78 (8.97%)			
occurrences (all)	9			
hypoaesthesia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	2 / 78 (2.56%)			
occurrences (all)	2			
nervous system disorder				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences (all)	2			
paraesthesia				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	0 / 78 (0.00%)			
occurrences (all)	0			
seizure				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	5 / 78 (6.41%)			
occurrences (all)	5			
somnolence				
alternative dictionary used: MedDRA 27.1				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences (all)	1			

tremor			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	3		
lymphopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	9 / 78 (11.54%)		
occurrences (all)	11		
neutropenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	8 / 78 (10.26%)		
occurrences (all)	10		
thrombocytopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	21 / 78 (26.92%)		
occurrences (all)	26		
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	7		
abdominal pain upper			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	3		
constipation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	7 / 78 (8.97%)		
occurrences (all)	9		
diarrhoea			

alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	8		
haemorrhoids			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 78 (0.00%)		
occurrences (all)	0		
nausea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	13 / 78 (16.67%)		
occurrences (all)	13		
stomatitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
vomiting			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	14 / 78 (17.95%)		
occurrences (all)	16		
Skin and subcutaneous tissue disorders			
dry skin			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
hirsutism			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[2]	0 / 20 (0.00%)		
occurrences (all)	0		
pruritus			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	5		
Renal and urinary disorders			

urinary incontinence alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all)	 2 / 78 (2.56%) 2		
Endocrine disorders cushingoid alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all)	 3 / 78 (3.85%) 3		
Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all) back pain alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all) muscular weakness alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all) myalgia alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all) neck pain alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all) pain in extremity alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all)	 6 / 78 (7.69%) 15 5 / 78 (6.41%) 6 4 / 78 (5.13%) 4 2 / 78 (2.56%) 7 1 / 78 (1.28%) 1 2 / 78 (2.56%) 2		
Infections and infestations			

urinary tract infection alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all)	 4 / 78 (5.13%) 4		
Metabolism and nutrition disorders hyperglycaemia alternative dictionary used: MedDRA 27.1 subjects affected / exposed occurrences (all)	 5 / 78 (6.41%) 5		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported