Clinical trial results:
A 2-part Phase III Randomized, Open Label, Multicenter Study of LGX818 Plus MEK162 Versus Vemurafenib and LGX818 Monotherapy in Patients With Unresectable or Metastatic BRAF V600 Mutant Melanoma

Summary

EudraCT number	2013-001176-38
Trial protocol	NL SE IT ES GB CZ SK HU NO FR GR PL PT
Global end of trial date	

Results information

Result version number	v1
This version publication date	14 July 2024
First version publication date	14 July 2024

Trial information

Trial identification

Sponsor protocol code	C4221004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01909453
WHO universal trial number (UTN)	-
Other trial identifiers	CMEK162B2301: Other Study ID

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	Interim
Date of interim/final analysis	17 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 November 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether treatment with Combo 450 prolongs PFS compared with vemurafenib, in subjects with BRAF V600 mutant locally advanced unresectable or metastatic melanoma

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Brazil: 26
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	France: 59
Country: Number of subjects enrolled	Germany: 194
Country: Number of subjects enrolled	Greece: 29
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 113
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Netherlands: 46
Country: Number of subjects enrolled	Norway: 7
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Portugal: 18
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Singapore: 2

Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Spain: 104
Country: Number of subjects enrolled	Sweden: 17
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Türkiye: 2
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	United States: 41
Country: Number of subjects enrolled	Czechia: 38
Worldwide total number of subjects	921
EEA total number of subjects	671

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)	661
From 65 to 84 years	254
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 921 subjects (577 in part 1 and 344 in part 2) were randomized in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)

Arm description:

Subjects received 450 milligram (mg) of LGX818 orally once daily (QD) along with 45 mg of MEK162 twice daily (BID) for in each 28 day treatment cycle until progressive disease (PD) as confirmed by Blinded Independent Review Committee (BIRC), withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Arm type	Experimental
Investigational medicinal product name	MEK162
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MEK162 45 mg twice a day in each 28-day treatment cycle, administered as 15 mg tablets.

Investigational medicinal product name	LGX818
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LGX818 450 mg once a day in each 28-day treatment cycle, administered as 100 mg and 50 mg capsules.

Arm title	Part 1: LGX818 300 mg

Arm description:

Subjects received 300 mg of LGX818 orally once daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Arm type	Experimental
Investigational medicinal product name	LGX818
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LGX818 300 mg once a day in each 28-day treatment cycle, administered as 100 mg and 50 mg capsules.

Arm title	Part 1: Vemurafenib 960 mg BID

Arm description:

Subjects received 960 mg of vemurafenib according to the locally approved prescribing information twice daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

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

Dosage and administration details:

Vemurafenib 960 mg twice a day in each 28-day treatment cycle, administered as 240 mg tablets.

Arm title	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)

Arm description:

Subjects received 300 mg of LGX818 orally once daily along with 45 mg of MEK162 twice daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Arm type	Experimental
Investigational medicinal product name	MEK162
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MEK162 45 mg twice a day in each 28-day treatment cycle, administered as 15 mg tablets.

Investigational medicinal product name	LGX818
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LGX818 300 mg once a day in each 28-day treatment cycle, administered as 100 mg and 50 mg capsules.

Arm title	Part 2: LGX818 300 mg

Arm description:

Subjects received 300 mg of LGX818 orally once daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Arm type	Experimental
Investigational medicinal product name	LGX818
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LGX818 300 mg once a day in each 28-day treatment cycle, administered as 100 mg and 50 mg capsules.

Number of subjects in period 1	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID
Started	192	194	191
Completed	1	2	0
Not completed	191	192	191
Adverse event, serious fatal	10	2	4
Physician decision	13	29	18
Study Terminated By Sponsor	2	1	-
Adverse event, non-fatal	25	26	26
Randomized but not treated	-	2	5
Progressive Disease	106	105	115
Treatment ongoing	13	3	2
Subject/Guardian Decision	20	23	20
Lost to follow-up	1	-	-
New Therapy For Study Indication	-	-	1
Protocol deviation	1	1	-

Number of subjects in period 1	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg
Started	258	86
Completed	2	0
Not completed	256	86
Adverse event, serious fatal	7	3
Physician decision	38	13
Study Terminated By Sponsor	3	-
Adverse event, non-fatal	35	8
Randomized but not treated	1	2
Progressive Disease	138	47
Treatment ongoing	17	2
Subject/Guardian Decision	17	10
Lost to follow-up	-	1
New Therapy For Study Indication	-	-
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)
Reporting group description:	
Subjects received 450 milligram (mg) of LGX818 orally once daily (QD) along with 45 mg of MEK162 twice daily (BID) for in each 28 day treatment cycle until progressive disease (PD) as confirmed by Blinded Independent Review Committee (BIRC), withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.	
Reporting group title	Part 1: LGX818 300 mg
Reporting group description:	
Subjects received 300 mg of LGX818 orally once daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.	
Reporting group title	Part 1: Vemurafenib 960 mg BID
Reporting group description:	
Subjects received 960 mg of vemurafenib according to the locally approved prescribing information twice daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.	
Reporting group title	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Reporting group description:	
Subjects received 300 mg of LGX818 orally once daily along with 45 mg of MEK162 twice daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.	
Reporting group title	Part 2: LGX818 300 mg
Reporting group description:	
Subjects received 300 mg of LGX818 orally once daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.	

Reporting group values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID
Number of subjects	192	194	191
Age Categorical Units: subjects			
<=18 years	0	0	0
Between 18 and 65 years	132	154	140
>=65 years	60	40	51
Sex: Female, Male Units: subjects			
Female	77	86	80
Male	115	108	111
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic/latino	20	33	14
Chinese	1	0	0
Japanese	3	3	5
Korean	1	2	2
Russian	10	8	5
Turkish	0	2	0
Mixed ethnicity	1	3	1

Other	131	116	129
Other South Asian	0	1	0
Other Southeast Asian	1	0	1
Unknown	18	23	25
Missing	6	3	9
Race (NIH/OMB) Units: Subjects			
Caucasian	180	175	168
Asian	5	6	8
Native American	0	2	2
Other	3	2	2
Uknown	3	9	11
Missing	1	0	0
Black	0	0	0

Reporting group values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Total
Number of subjects	258	86	921
Age Categorical Units: subjects			
<=18 years	0	0	0
Between 18 and 65 years	175	60	661
>=65 years	83	26	260
Sex: Female, Male Units: subjects			
Female	107	42	392
Male	151	44	529
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic/latino	41	12	120
Chinese	0	0	1
Japanese	7	3	21
Korean	8	4	17
Russian	12	7	42
Turkish	1	0	3
Mixed ethnicity	2	0	7
Other	158	44	578
Other South Asian	0	0	1
Other Southeast Asian	0	0	2
Unknown	22	9	97
Missing	7	7	32
Race (NIH/OMB) Units: Subjects			
Caucasian	236	79	838
Asian	15	7	41
Native American	0	0	4
Other	2	0	9
Uknown	4	0	27
Missing	0	0	1
Black	1	0	1

End points reporting groups

Reporting group title	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)

Reporting group description:

Subjects received 450 milligram (mg) of LGX818 orally once daily (QD) along with 45 mg of MEK162 twice daily (BID) for in each 28 day treatment cycle until progressive disease (PD) as confirmed by Blinded Independent Review Committee (BIRC), withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 1: LGX818 300 mg

Reporting group description:

Subjects received 300 mg of LGX818 orally once daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 1: Vemurafenib 960 mg BID

Reporting group description:

Subjects received 960 mg of vemurafenib according to the locally approved prescribing information twice daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)

Reporting group description:

Subjects received 300 mg of LGX818 orally once daily along with 45 mg of MEK162 twice daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 2: LGX818 300 mg

Reporting group description:

Subjects received 300 mg of LGX818 orally once daily in each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Subject analysis set title	Part 1 + Part 2: LGX818 300 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects of Part 1 and 2 received 300 mg of LGX818 orally once daily for each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, and study discontinuation, lost to follow-up or death.

Primary: Part 1: Progression Free Survival (PFS) by Blinded Independent Review Committee (BIRC) in Combo 450 Group as Compared to Vemurafenib Group

End point title	Part 1: Progression Free Survival (PFS) by Blinded Independent Review Committee (BIRC) in Combo 450 Group as Compared to Vemurafenib Group[1][2]

End point description:

PFS was defined as the time from the date of randomization to the date of the first documented disease progression (PD) or death due to any cause, whichever occured first. PFS was determined based on tumor assessment (RECIST version 1.1 criteria) as per BIRC/central review and survival information. If a subject did not have an event at the time of the analysis cut-off or at the start of any new anti-cancer therapy, data was censored at the date of last adequate tumor assessment. PD was defined as at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must demonstrate an absolute increase of at least 5 square millimeter (mm^2). Full analysis set (FAS) included all randomized subjects.

End point type	Primary

End point timeframe:

From randomization until documented disease progression (PD), initiation of new anti-cancer therapy, censoring date or death, whichever occurred first (up to 29 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: This endpoint was summarized for specified reporting arms only.

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

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: Vemurafenib 960 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	191		
Units: months				
median (confidence interval 95%)	14.9 (11.0 to 20.2)	7.3 (5.6 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: PFS by BIRC in Combo 450 Group as Compared to LGX818 Group

End point title	Part 1: PFS by BIRC in Combo 450 Group as Compared to LGX818 Group[3][4]

End point description:

PFS was defined as the time from the date of randomization to the date of the first documented PD or death due to any cause, whichever occured first. PFS was determined based on tumor assessment (RECIST version 1.1 criteria) as per BIRC and survival information. If a subject did not have an event at the time of the analysis cut-off or at the start of any new anti-cancer therapy, data was censored at the date of last adequate tumor assessment. PD was defined as at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must demonstrate an absolute increase of at least 5 mm^2. FAS included all randomized subjects.

End point type	Primary

End point timeframe:

From randomization until documented PD, initiation of new anti-cancer therapy, censoring date or death, whichever occurred first (up to 29 months), excluding Part 1: LGX818 300 mg group; up to 35 months for Part 1: LGX 300 mg group

Notes:

[3] - 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: This endpoint was summarized for specified reporting arms only.

[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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	194		
Units: months				

median (confidence interval 95%)	14.9 (11.0 to 20.2)	9.6 (7.4 to 14.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: PFS by BIRC in Combo 300 Group as Compared to LGX818 Group

End point title	Part 2: PFS by BIRC in Combo 300 Group as Compared to LGX818 Group[5]

End point description:

PFS was defined as the time from the date of randomization to the date of the first documented disease progression (PD) or death due to any cause, whichever occurs first. PFS was determined based on tumor assessment (RECIST version 1.1 criteria) as per BIRC and survival information. If a subject did not had an event at the time of the analysis cut-off or at the start of any new anti-cancer therapy, data was censored at the date of last adequate tumor assessment. PD was defined as at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must demonstrate an absolute increase of at least 5 mm^2. FAS included all randomized subjects. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

From randomization until documented PD, initiation of new anti-cancer therapy, censoring date or death, whichever occurred first (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

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

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	258	86	280	
Units: months				
median (confidence interval 95%)	12.9 (10.9 to 14.9)	7.4 (5.6 to 9.2)	9.2 (7.4 to 11.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Subject With Adverse Events (AEs) and Serious Adverse Events (SAEs) as Graded by National Cancer Institute Common Terminology Criteria (NCI-CTCAE), Version 4.03

End point title	Part 1: Percentage of Subject With Adverse Events (AEs) and Serious Adverse Events (SAEs) as Graded by National Cancer Institute Common Terminology Criteria (NCI-CTCAE), Version 4.03[6]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was any untoward medical occurrence at any dose that resulted in death; was life-threatening; required inpatient hospitalization/prolongation of existing hospitalization; results in persistent/significant disability/incapacity; resulted in congenital anomaly/birth defect or important medical event. Per NCI-CTCAE v4.03, severity was graded as Grade(G)1: asymptomatic/mild symptoms; G2: moderate; G3: severe/medically significant; G4: life-threatening consequence; G5: death. AEs of all grades were reported. Safety analysis set=all subjects who received at least one dose of study medication and had at least one valid post-baseline safety evaluation. Number of subjects analyzed=number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: percentage of subjects				
number (not applicable)				
Subjects with AEs	98.4	99.5	100	
Subjects with SAEs	44.3	37.0	41.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Overall Survival (OS)

End point title	Part 1: Overall Survival (OS)[7]

End point description:

Overall survival was defined as the time from the date of randomization to the date of death due to any cause. If a death had not been observed by the date of analysis cutoff, OS was censored at the date of last contact. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

From randomization until date of death or censoring date whichever occurred first (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

Notes:

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

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	194	191	
Units: months				
median (confidence interval 95%)	33.6 (24.4 to 39.2)	23.5 (19.6 to 33.6)	16.9 (14.0 to 24.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Subjects With Clinically Notable Shift From Baseline in Laboratory Parameter Values Based on NCI-CTCAE Grade, Version 4.03

End point title	Part 1: Number of Subjects With Clinically Notable Shift From Baseline in Laboratory Parameter Values Based on NCI-CTCAE Grade, Version 4.03[8]

End point description:

Number of subjects with clinically notable shift from baseline in laboratory parameter values based on NCI-CTCAE grade, Version 4.03 where Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2: Moderate; minimal, local or non-invasive intervention indicated. Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated. Grade 4: Life-threatening consequences; urgent intervention indicated. Grade 5: Death. Clinically notable shift from baseline in laboratory parameter = worsening by at least 2 grades or to >=grade 3. Safety analysis set included all subjects who received at least one dose of study medication and have at least one valid post-baseline safety evaluation. Number of subjects analyzed signifies the number of subjects evaluable for this endpoint. n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

Notes:

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

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: subjects				
Hemoglobin (hypo) (n=192,186,192)	28	12	17	
Hemoglobin (hyper) (n=192,186,192)	0	1	0	
Leukocytes (hypo) (n=192,186,192)	8	4	4	
Lymphocytes (hypo) (n=191,186,192)	30	21	42	
Lymphocytes (hyper) (n=191,186,192)	15	11	6	
Neutrophils (hypo) (n=192,186,192)	20	7	3	
Platelets (hypo) (n=192,186,192)	3	4	1	

Prothrombin INR (hyper) (n=188,181,180)	0	1	2	
Alanine Aminotransferase (hyper) (n=192,186,192)	16	8	8	
Albumin (hypo) (n=192,186,192)	5	5	2	
Alkaline Phosphatase (hyper) (n=192,186,192)	8	3	4	
Aspartate Aminotransferase (hyper) (n=192,186,192)	12	4	5	
Bilirubin (hyper) (n=192,186,192)	1	0	15	
Corrected Calcium (hypo) (n=191,186,192)	3	3	3	
Corrected Calcium (hyper) (n=191,186,192)	1	1	2	
Creatinine kinase (hyper) (n=190,186,191)	41	2	2	
Creatinine (hyper) (n=192,186,192)	48	17	52	
Fasting glucose (hypo) (n=149,125,155)	2	4	3	
Fasting glucose (hyper) (n=149,125,155)	26	14	11	
Gamma glutamyl transferase (hyper) (n=191,186,192)	45	30	15	
Magnesium (hyper) (n=190,186,192)	2	3	1	
Phosphate (hypo) (n=190,186,192)	30	25	35	
Potassium (hypo) (n=192,186,192)	2	1	3	
Potassium (hyper) (n=192,186,192)	12	6	6	
Sodium (hypo) (n=192,186,192)	10	1	1	
Sodium (hyper) (n=192,186,192)	1	1	0	
Urate (hyper) (n=191,186,191)	2	3	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Subjects With Newly Occurring Notable Abnormal Vital Signs

End point title	Part 1: Number of Subjects With Newly Occurring Notable Abnormal Vital Signs[9]

End point description:

Notable abnormal vital signs were: Low/high systolic blood pressure (SBP) (millimeter of mercury [mmHg]): less than or equal to (<=) 90 mmHg with decrease from baseline of greater than or equal to (>=) 20 mmHg/>= 160 mmHg with increase from baseline of >=20 mmHg. Low/high diastolic blood pressure (DBP) [mmHg]: <= 50 mmHg with decrease from baseline of >=15 mmHg/>=100 mmHg with increase from baseline of >=15 mmHg. Low/high Pulse rate: <=50 beats per minute (bpm) with decrease from baseline of >=15 bpm/>= 120 bpm with increase from baseline of >=15 bpm. Low/high Weight [kilogram]: >=20 percent (%) decrease from baseline/>= 10% increase from baseline. Low/high Body temperature degree Celsius (C): <= 36 degree C/>= 37.5 degree C. Safety analysis set was used. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: subjects				
Sitting Pulse Rate (bpm): High (n=184,182,186)	3	7	9	
Sitting Pulse Rate (bpm): Low (n=181,182,185)	6	10	4	
Sitting SBP (mmHg): High (n=177,173,177)	37	17	33	
Sitting SBP (mmHg): Low (n=184,182,188)	10	4	1	
Sitting DBP(mmHg): High (n=183,181,182)	34	8	14	
Sitting DBP (mmHg): Low (n=185,184,188)	11	11	6	
Weight (kg): High (n=184,184,187)	55	11	8	
Weight (kg): Low (n=184,184,187)	4	10	13	
Body temperature (degree C): High (n=176,181,185)	23	14	18	
Body temperature (degree C): Low (n=134,141,132)	81	75	59	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Subjects With Newly Occurring Notable Electrocardiogram (ECG) Values

End point title	Part 1: Number of Subjects With Newly Occurring Notable Electrocardiogram (ECG) Values[10]

End point description:

Newly occurring notable ECG values were reported for QT (ms[millisecond]), QTcF, QT interval corrected for heart rate using Fridericia's formula (ms), QTcB, QT interval corrected for heart rate using Bazett's formula (ms) and heart rate (bpm). Newly occurring was defined as subjects not meeting criterion at baseline and meeting criterion post-baseline. Ranges for newly occurring notable ECG values (QT, QTcF, QTcB) are New >450, New >480, New >500, increase (inc.) from baseline >30, Increase from baseline >60. Heart rate: New < 60, New >100 was considered as newly occurring notable value. Safety analysis set included all subjects who received at least one dose of study medication and had at least one valid post-baseline safety evaluation. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: subjects				
QT: Increase >30 ms (181,179,187)	113	74	84	
QT: Increase >60 ms (181,179,187)	32	24	28	
QT: New >450 ms (170,173,180)	28	21	22	
QT: New >480 ms (n=177,178,187)	5	7	3	
QT: New >500 ms (n=179,179,187)	2	4	2	
QTcF: Increase >30 ms (n=180,179,186)	60	62	76	
QTcF: Increase >60 ms (n=180,179,186)	11	11	13	
QTcF: New >450 ms (n=172,174,178)	33	42	42	
QTcF: New >480 ms (n=178,179,186)	7	10	6	
QTcF: New >500 ms (n=179,179,186)	1	7	3	
QTcB: Increase >30 ms (n=180,177,184)	60	79	79	
QTcB: Increase >60 ms (n=180,177,184)	14	19	16	
QTcB: New >450 ms (n=159,155,155)	54	78	66	
QTcB: New >480 ms (n=175,176183)	17	28	20	
QTcB: New >500 ms (n=180,177,183)	4	13	10	
Heart rate: New <60 bpm(n=159,153,163)	62	38	21	
Heart rate: New <100 bpm(n=175,170,182)	19	24	20	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Subjects With Worst Post-baseline Left Ventricular Dysfunction Events (LVEF) Values by Multigated Acquisition (MUGA) Scans or Transthoracic Echocardiograms (ECHO), by CTCAE Grade

End point title	Part 1: Number of Subjects With Worst Post-baseline Left Ventricular Dysfunction Events (LVEF) Values by Multigated Acquisition (MUGA) Scans or Transthoracic Echocardiograms (ECHO), by CTCAE Grade[11]

End point description:

Subjects with worst post-baseline LVEF Values were graded as Grade 0: Non missing value below Grade 2; Grade 2: LVEF between 40% and 50% or absolute reduction from baseline >=10% and < 20%; Grade 3: LVEF between 20% and 39% or absolute reduction from baseline >=20%; Grade 4: LVEF lower than 20%. Baseline was defined as the last non-missing value prior to the first dose of study treatment. Missing data were due to subjects who died or withdrew consent prior to the first scheduled evaluation or missed evaluations as protocol deviations. Safety analysis set included all subjects who

received at least one dose of study medication and had at least one valid post-baseline safety evaluation. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: subjects				
Grade 0	120	159	160	
Grade 2	62	18	17	
Grade 3	4	5	2	
Grade 4	0	0	0	
Missing	6	10	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Subjects With Dermatologic-Related Adverse Events of Special Interest (AESI) Graded According to the NCI-CTCAE Version 4.03

End point title	Part 1: Number of Subjects With Dermatologic-Related Adverse Events of Special Interest (AESI) Graded According to the NCI-CTCAE Version 4.03[12]

End point description:

AESI consisted of events for which there was a specific clinical interest with regard to LGX818 and/or MEK162 treatment. Dermatologic-related AESI included severe cutaneous adverse reactions. As per NCI-CTCAE version 4.03, severity was graded as Grade 1: asymptomatic/mild symptoms, clinical/diagnostic observations only, intervention not indicated; Grade 2: moderate, minimal, local/noninvasive intervention indicated, limiting age-appropriate instrumental ADL; Grade 3: severe/medically significant but not immediately life-threatening, hospitalization/prolongation of existing hospitalization indicated, disabling, limiting self-care ADL; Grade 4: life-threatening consequence, urgent intervention indicated; Grade 5: death related to AE. AEs of grade 3 or 4 are reported in this endpoint. Safety analysis set. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

Notes:

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

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: subjects				
Severe cutaneous adverse reactions	2	2	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Subjects With Ocular-Related AESI Graded According to the NCI-CTCAE Version 4.03

End point title	Part 1: Number of Subjects With Ocular-Related AESI Graded According to the NCI-CTCAE Version 4.03[13]

End point description:

AESI consisted of events for which there was a specific clinical interest with regard to LGX818 and/or MEK162 treatment. Ocular-related AESI included uveitis-type events. As per NCI-CTCAE version 4.03, severity was graded as Grade 1: asymptomatic/mild symptoms, clinical/diagnostic observations only, intervention not indicated; Grade 2: moderate, minimal, local/noninvasive intervention indicated, limiting age-appropriate instrumental ADL; Grade 3: severe/medically significant but not immediately life-threatening, hospitalization/prolongation of existing hospitalization indicated, disabling, limiting self-care ADL; Grade 4: life-threatening consequence, urgent intervention indicated; Grade 5: death related to AE. AEs of grade 3 or 4 are reported in this endpoint. Safety analysis set. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 471.7, 471.4 and 465.4 weeks of treatment for Combo450, LGX818 300 and vemurafenib arms, respectively)

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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	192	186	
Units: subjects				
Uveitis-type events	11	2	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Subjects With AEs and SAEs as Graded by NCI-CTCAE Version 4.03

End point title	Part 2: Percentage of Subjects With AEs and SAEs as Graded by NCI-CTCAE Version 4.03[14]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was any untoward medical occurrence at any dose that results in death; is life-threatening; requires inpatient hospitalization/prolongation of existing hospitalization; results in persistent/significant disability/incapacity; results in congenital anomaly/birth defect or that is considered to be important medical event. Per NCI-CTCAE v4.03, severity was graded as G1: asymptomatic/mild symptoms; G2: moderate; G3: severe/medically significant; G4: life-threatening consequence; G5: death. AEs of all grades were reported. Safety analysis set was used. 'Number of subjects analyzed' =number of subjects evaluable for this endpoint. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

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

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	257	84	276	
Units: percentage of subjects				
number (not applicable)				
AEs	98.4	97.6	98.9	
SAEs	38.1	36.9	37.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Subjects With Clinically Notable Shift From Baseline in Laboratory Parameter Values Based on NCI-CTCAE Grade, Version 4.0

End point title	Part 2: Number of Subjects With Clinically Notable Shift From Baseline in Laboratory Parameter Values Based on NCI-CTCAE Grade, Version 4.0[15]

End point description:

Number of subjects with clinically notable shift from baseline in laboratory parameter values based on NCI-CTCAE grade, Version 4.03 where, Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2: Moderate; minimal, local or noninvasive intervention indicated. Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated. Grade 4: Life-threatening consequences; urgent intervention indicated. Grade 5: Death. Clinically notable shift from baseline in laboratory parameter = worsening by at least 2 grades or to >=grade 3. Safety analysis set was used. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

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

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	257	84	276	
Units: subjects				
Hemoglobin (hypo) (n=257,84,276)	23	6	18	
Prothrombin INR (hyper) (n=246,80,268)	5	0	1	
Lymphocytes (hypo) (n=257,84,275)	44	13	34	
Lymphocytes (hyper) (n=257,84,275)	13	3	14	
Neutrophils (hypo) (n=257,84,276)	35	6	13	
Platelets (hypo) (n=256,84,276)	3	1	5	
Leukocytes (hypo) (n=257,84,276)	16	3	7	
Albumin (hypo) (n=257,84,276)	9	4	9	
Alkaline phosphatase (hyper) (n=257,84,276)	12	2	5	
Alanine aminotransferase (hyper) (n=257,84,276)	20	1	9	
Aspartate aminotransferase (hyper) (n=257,84,276)	17	1	5	
Bilirubin (hyper) (n=257,84,276)	4	0	0	
Creatine kinase (hyper) (n=257,84,274)	57	1	3	
Corrected Calcium (hypo) (n=257,84,275)	5	2	5	
Creatinine (hyper) (n=257,84,276)	65	14	31	
Gamma-glutamyl transferase(hyper) (n=257,84,257)	45	7	37	
Fasting Glucose (hypo) (n=207,67,216)	5	0	4	
Fasting Glucose (hyper) (n=207,67,216)	29	4	18	
Corrected Calcium (hyper) (n=257,84,275)	4	0	1	
Magnesium (hyper) (n=257,84,274)	3	0	3	
Phosphate (hypo) (n=257,84,274)	34	10	35	
Potassium (hypo) (n=257,84)	2	1	2	
Potassium (hyper) (n=257,84,276)	13	3	9	
Sodium (hypo) (n=257,84,276)	6	2	3	
Sodium (hyper) (n=257,84,276)	3	0	1	
Urate (hyper) (n=257,84,275)	3	1	4	
Hemoglobin (hyper) (n=257,84,276)	2	0	1	
Activated partial TP time (hyper) (n=246,80,268)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Subjects With Newly Occurring Notable Abnormal Vital Signs

End point title	Part 2: Number of Subjects With Newly Occurring Notable Abnormal Vital Signs[16]

End point description:

Notable abnormal vital signs were: Low/high SBP in mmHg: <= 90 mmHg with decrease from baseline of >= 20 mmHg/>= 160 mmHg with increase from baseline of >=20 mmHg, Low/high DBP [mmHg]: <=50 mmHg with decrease from baseline of >=15 mmHg/>=100 mmHg with increase from baseline of >=15 mmHg, Low/high pulse rate [bpm]: <=50 bpm with decrease from baseline of >=15 bpm/>=120 bpm with increase from baseline of >=15 bpm, Low/high weight (kg): >=20 % decrease from baseline/>= 10% increase from baseline Low/high Body temperature degree C: <= 36 degree C/>= 37.5 degree C. Safety analysis set was used. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

[16] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	257	84	276	
Units: subjects				
Sitting Pulse Rate (bpm): High (n=252,78,262)	10	3	10	
Sitting Pulse Rate (bpm): Low(n=254,77,258)	16	1	11	
Sitting SBP (mmHg): High (n=243,76,253)	51	5	22	
Sitting SBP (mmHg): Low (n=255,78,262)	15	5	9	
Sitting DBP (mmHg): High (n=253,78,261)	49	6	14	
Sitting DBP (mmHg): Low(n=255,77,262)	12	2	13	
Weight (kg): High(n=256,80,264)	58	3	14	
Weight (kg): Low (n=256,80,264)	0	1	11	
Body temperature (°C): High(n=252,77,253)	24	5	19	
Body temperature (°C): Low(n=201,55,189)	128	23	98	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Subjects With Newly Occurring Notable ECG Values

End point title	Part 2: Number of Subjects With Newly Occurring Notable ECG Values[17]

End point description:

Newly occurring notable ECG values were reported for QT (ms), QTcF (ms), QTcB (ms) and heart rate (bpm). Newly occurring was defined as subjects not meeting criterion at baseline and meeting criterion post-baseline. Ranges for newly occurring notable ECG values (QT, QTcF, QTcB) are New >450, New >480, New >500, increase (inc.) from baseline >30, Increase from baseline >60. Heart rate: New < 60, New >100 was considered as newly occurring notable value. Safety analysis set included all subjects who received at least one dose of study medication and had at least one valid post-baseline safety evaluation. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

[17] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	257	84	276	
Units: subjects				
QT (ms): Inc. from baseline > 30 (n=251,79,260)	146	35	109	
QT (ms): Inc. from baseline > 60 (n=251,79,260)	45	7	31	
QT (ms): New > 450 (n=239,76,246)	44	8	29	
QT (ms): New > 480 (n=249,79,256)	12	2	9	
QT (ms): New > 500 (n=251,79,258)	5	0	4	
QTcF (ms): Inc. from baseline > 30 (n=250,78,258)	81	24	86	
QTcF (ms): Inc. from baseline > 60 (n=250,78,258)	17	8	19	
QTcF (ms): New > 450 (n=240,70,242)	46	15	57	
QTcF (ms): New > 480 (n=249,78,256)	16	7	17	
QTcF (ms): New > 500 (n=250,78,257)	2	1	8	
QTcB (ms): New > 450 (n=216,67,226)	87	31	109	
QTcB (ms): New > 480 (n=247,77,252)	28	6	34	
QTcB (ms): New > 500(n=250,79,259)	13	2	15	
QTcB (ms): Inc. from baseline > 30(n=250,79,259)	87	26	105	
QTcB (ms): Inc. from baseline > 60(n=250,79,259)	26	9	28	
Heart rate (bpm): New < 60(n=213,67,226)	88	7	45	
Heart rate (bpm): New > 100(n=241,74,249)	12	11	35	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Subjects With Worst Post-baseline LVEF Values by MUGA Scans or Transthoracic ECHO, by CTCAE Grade

End point title	Part 2: Number of Subjects With Worst Post-baseline LVEF Values by MUGA Scans or Transthoracic ECHO, by CTCAE Grade[18]

End point description:

Subjects with worst post-baseline LVEF Values were graded as Grade 0: Non missing value below Grade 2; Grade 2: LVEF between 40% and 50% or absolute reduction from baseline >=10% and < 20%;Grade 3: LVEF between 20% and 39% or absolute reduction from baseline >=20%; Grade 4: LVEF lower than 20%. Baseline was defined as the last non-missing value prior to the first dose of study treatment. Missing data were due to subjects who died or withdrew consent prior to the first scheduled evaluation or missed evaluations as protocol deviations. Safety analysis set included all subjects who received at least one dose of study medication and had at least one valid post-baseline safety evaluation. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

[18] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	257	84	276	
Units: subjects				
Grade 0	172	70	229	
Grade 2	77	9	27	
Grade 3	6	0	5	
Grade 4	0	0	0	
Missing	2	5	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Subjects With Dermatologic-Related AESI Graded According to the NCI-CTCAE Version 4.03

End point title	Part 2: Number of Subjects With Dermatologic-Related AESI Graded According to the NCI-CTCAE Version 4.03[19]

End point description:

AESI consisted of events for which there was a specific clinical interest with regard to LGX818 and/or MEK162 treatment. Dermatologic-related AESI included severe cutaneous adverse reactions. As per NCI-CTCAE version 4.03, severity was graded as Grade(G) 1: asymptomatic/mild symptoms, clinical/diagnostic observations only, intervention not indicated; G2: moderate, minimal, local/noninvasive intervention indicated, limiting age-appropriate instrumental ADL; G3: severe/medically significant but not immediately life-threatening, hospitalization/prolongation of existing hospitalization indicated, disabling, limiting self-care ADL; G4: life-threatening consequence, urgent intervention indicated; G5: death related to AE. AEs of G3/4 are reported are reported in this endpoint. Safety analysis set. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

[19] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 300 mg	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	192	257	84	276
Units: subjects				
Cutaneous adverse reactions	2	4	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Subjects With Ocular-Related AESI Graded According to the NCI-CTCAE Version 4.03

End point title	Part 2: Number of Subjects With Ocular-Related AESI Graded According to the NCI-CTCAE Version 4.03[20]

End point description:

AESI consisted of events for which there was a specific clinical interest with regard to LGX818 and/or MEK162 treatment. Ocular-related AESI included uveitis-type events. As per NCI-CTCAE version 4.03, severity was graded as Grade 1: asymptomatic/mild symptoms, clinical/diagnostic observations only, intervention not indicated; Grade 2: moderate, minimal, local/noninvasive intervention indicated, limiting age-appropriate instrumental ADL; Grade 3: severe/medically significant but not immediately life-threatening, hospitalization/prolongation of existing hospitalization indicated, disabling, limiting self-care ADL; Grade 4: life-threatening consequence, urgent intervention indicated; Grade 5: death related to AE. AEs of grade 3 or 4 are reported in this endpoint. Safety analysis set. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

[20] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 300 mg	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	192	257	84	276
Units: subjects				
Uveitis-type events	2	15	1	3

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Objective Response Rate (ORR)

End point title	Part 1 and Part 2: Objective Response Rate (ORR)

End point description:

ORR, calculated as the percentage of subjects with a best overall response of complete response (CR) or partial response (PR). CR was defined as disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm. PR was defined as at least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. Results are reported for confirmed BIRC response. FAS included all randomized subjects. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

From randomization until disease progression, censoring date or death, whichever occurred first(up to maximum of 417.7, 465.4, 471.4, 471.4 and 415.4 weeks of treatment for LGX818 300, vemurafenib, combo 300, combo 450 and Part 1 and 2 arms, respectively

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	194	191	258
Units: percentage of subjects				
number (confidence interval 95%)	64.1 (56.8 to 70.8)	51.5 (44.3 to 58.8)	40.8 (33.8 to 48.2)	67.8 (61.8 to 73.5)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	86	280		
Units: percentage of subjects				
number (confidence interval 95%)	51.2 (40.1 to 62.1)	51.4 (45.4 to 57.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Overall Survival (OS)

End point title	Part 2: Overall Survival (OS)[21]

End point description:

Overall survival was defined as the time from the date of randomization to the date of death due to any cause. If a death had not been observed by the date of analysis cutoff, OS was censored at the date of last contact. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

From randomization until date of death or censoring date, whichever occurred first (up to maximum of 417.7 and 471.4 weeks of treatment for Combo 300 and LGX818 300 respectively)

Notes:

[21] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	86		
Units: Months				
median (confidence interval 95%)	27.1 (21.6 to 33.3)	19.4 (14.5 to 28.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Disease Control Rate (DCR)

End point title	Part 1 and Part 2: Disease Control Rate (DCR)

End point description:

DCR was calculated as the percentage of subjects with a best overall response (BOR) of CR, PR, or stable disease (SD). CR was defined as disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. Two sets of DCR were considered, one for confirmed and one for unconfirmed responses. Results are reported for confirmed and unconfirmed responses combined. SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for PD. DCR was based on central review. FAS included all randomized subjects. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

From randomization until disease progression or death, whichever occurred first (up to 111 months)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	192	194	191	258
Units: percentage of subjects				
number (confidence interval 95%)	92.2 (87.4 to 95.6)	84.0 (78.1 to 88.9)	81.2 (74.9 to 86.4)	90.7 (86.5 to 93.9)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	86	280		
Units: percentage of subjects				
number (confidence interval 95%)	79.1 (69.0 to 87.1)	82.5 (77.5 to 86.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Time to Objective Response (TTR)

End point title	Part 1 and Part 2: Time to Objective Response (TTR)

End point description:

TTR was the time between date of randomization until first documented response of CR or PR. Subjects who did not achieve a PR or CR were censored at the last adequate tumor assessment date when they did not have a PFS event or at maximum follow-up (i.e. first patient first visit [FPFV] to last patient last visit [LPLV] used for the analysis) when they had a PFS event. CR was defined as disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. TTR was estimated in the treatment arms using a Kaplan-Meier method. TTR was based on central review. FAS included all randomized subjects. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

From randomization until disease progression, censoring date or death, whichever occurred first(up to maximum of 417.7, 465.4, 471.4, 471.4 and 415.4 weeks of treatment for LGX818 300, vemurafenib, combo 300, combo 450 and Part 1 and 2 arms, respectively)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	192	194	191	258
Units: months				
median (confidence interval 95%)	1.9 (1.9 to 1.9)	2.0 (1.9 to 3.6)	2.2 (1.9 to 3.8)	1.9 (1.9 to 1.9)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	86	280		
Units: months				
median (confidence interval 95%)	1.9 (1.9 to 2.3)	1.9 (1.9 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Duration of Response (DOR)

End point title	Part 1 and Part 2: Duration of Response (DOR)

End point description:

DOR was calculated, as time from date of first documented response(CR/PR) to the first documented progression/death due to underlying cancer. DOR was estimated for responders(i.e. subjects achieving at least once CR/PR) only using a Kaplan-Meier method. CR=disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm. PR=at least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. If a subject with CR/PR had no progression or death due to underlying disease, the subject was censored at the date of last adequate tumor assessment. Results are based on confirmed BIRC response. Analysis population included all the subjects who achieved at least once confirmed CR/PR. Number of subjects analyzed = number of subjects evaluable for this endpoint. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

From randomization until disease progression, censoring date or death, whichever occurred first(up to maximum of 417.7, 465.4, 471.4, 471.4 and 415.4 weeks of treatment for LGX818 300, vemurafenib, combo 300, combo 450 and Part 1 and 2 arms, respectively)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	100	78	175
Units: months				
median (confidence interval 95%)	18.6 (12.7 to 27.6)	15.5 (11.1 to 29.5)	12.3 (6.9 to 14.5)	15.4 (11.8 to 20.6)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	144		
Units: months				
median (confidence interval 95%)	11.0 (7.3 to 17.1)	14.8 (11.0 to 21.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Time to Definitive 10% Deterioration in the Function Assessment Cancer Therapy-melanoma (FACT-M) Subscale

End point title	Part 1 and Part 2: Time to Definitive 10% Deterioration in the Function Assessment Cancer Therapy-melanoma (FACT-M) Subscale

End point description:

FACT-M:melanoma specific questionnaire to assess subject health-related quality of life(QOL). Melanoma specific subscale consists of 16 items related to signs,symptoms,physical/social activities most relevant to subjects with advanced-stage melanoma. Other items include physical,functional&social/family well-being(7items each),emotional(6items). Each item range- 0(not at all) to 4(very much), combined to produce subscale scores.Total score range for FACT-M:0to172,higher scores:better QOL.Melanoma subscale score range from 0(worst response)to64(best response),higher score:better QOL. Time to definitive 10% deterioration:time from date of randomization to date of event with at least 10% relative to baseline worsening of corresponding scale score with no later improvement/death due to any cause. FAS included all randomized subjects. 99999-data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1 Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Date of randomization to date of event or death due to any cause, which ever occurred first (up to 29 months for Part 1, excluding Part 1: LGX818 300 mg group; up to 35 months for Part 2 and Part 1 LGX 300 mg group)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	192	194	191	258
Units: months				
median (confidence interval 95%)	99999 (22.1 to 99999)	30.5 (18.4 to 30.5)	22.1 (15.2 to 99999)	99999 (99999 to 99999)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	86	280		
Units: months				
median (confidence interval 95%)	99999 (9.4 to 99999)	20.5 (16.6 to 30.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Time to Definitive 10% Deterioration in the Global Health Status Score of the European Organization for Research and Treatment of Cancer's Core quality of Life Questionnaire (EORTC QLQ-C30)

End point title	Part 1 and Part 2: Time to Definitive 10% Deterioration in the Global Health Status Score of the European Organization for Research and Treatment of Cancer's Core quality of Life Questionnaire (EORTC QLQ-C30)

End point description:

EORTC QLQ-C30 is 30 item questionnaire composed of 5multi-item functional subscales(physical,role, cognitive,emotional,social functioning), 3symptom scales(fatigue,nausea/vomiting&pain),global health/QOL subscale&6single items assessing other cancer related symptoms(dyspnea,sleep disturbance,appetite,diarrhea, constipation&financial impact of cancer). It employed 28-four point Likert scales with responses from"not at all"to"very much"&two 7point Likert scales for global health&overall QOL. Global health status scale score ranged from 0-100. Higher score: better level of functioning. Time to definitive 10% deterioration: time from date of randomization to date of event with at least 10% relative to baseline worsening of corresponding scale score with no later improvement/death due to any cause. FAS included all randomized subjects. 99999: data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1&Part 2 for LGX818 300mg arm.

End point type	Secondary

End point timeframe:

Date of randomization to date of event or death due to any cause, which ever occurred first (maximum up to 29 months for Part 1, excluding Part 1: LGX818 300 mg group; up to 35 months for Part 2 and Part 1 LGX 300 mg group)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	192	194	191	258
Units: months				
median (confidence interval 95%)	23.9 (20.4 to 99999)	14.7 (8.1 to 24.0)	16.6 (11.9 to 99999)	18.4 (16.8 to 19.1)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	86	280		
Units: months				
median (confidence interval 95%)	9.5 (5.6 to 99999)	11.1 (7.7 to 20.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Change From Baseline in the Function Assessment Cancer Therapy-melanoma (FACT-M) Subscale at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point title	Part 1 and Part 2: Change From Baseline in the Function Assessment Cancer Therapy-melanoma (FACT-M) Subscale at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point description:

FACT-M: melanoma specific questionnaire to assess subject health-related QOL. Melanoma specific subscale consists of 16items related to signs, symptoms, physical/social activities most relevant to subjects with advanced-stage melanoma. Other items include physical, functional and social/family well-being (7items each), emotional well-being (6 items). Each item range from 0(not at all) to 4(very much), combined to produce subscale scores. Total score range for FACT-M-0 to 172, higher scores represented better quality of life. Melanoma subscale score range from 0(worst response) to 64(best response), higher score indicated better quality of life. FAS included all randomized subjects. Number of subjects analyzed = number of subjects evaluable for this endpoint. n= subjects with available data for each specified category. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1 and Part 2 for LGX818 300mg arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and end of treatment visit (within14 days after the last dose of study drug)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	165	177	159	234
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=177,159,234,83,165,260)	52.39 (± 9.053)	52.76 (± 8.206)	52.01 (± 8.650)	52.08 (± 8.493)
Change at C3 D1 (n=148,128,212,67,141,215)	0.92 (± 9.539)	-3.58 (± 8.133)	-1.55 (± 9.023)	2.79 (± 7.296)
Change at C5 D1 (n=132,106,200,60,128,192)	-0.01 (± 9.157)	-3.77 (± 7.576)	-1.90 (± 7.572)	2.58 (± 7.244)
Change at C7 D1 (n=109,84,177,52,120,161)	1.35 (± 9.595)	-3.05 (± 6.633)	-2.19 (± 8.651)	2.64 (± 7.766)
Change at C9 D1 (n=79,63,161,41,103,120)	0.52 (± 9.096)	-2.69 (± 6.513)	-1.90 (± 7.491)	3.23 (± 7.720)
Change at C11 D1(n=72,46,143,31,87,103)	0.18 (± 7.768)	-3.67 (± 6.418)	-0.51 (± 7.436)	2.54 (± 7.796)
Change at C13 D1(n=65,39,126,26,77,91)	-0.33 (± 8.855)	-2.71 (± 7.187)	-0.97 (± 8.818)	1.97 (± 8.127)
Change at C15 D1(n=56,29,95,18,68,74)	0.40 (± 7.943)	-2.48 (± 6.829)	-1.72 (± 9.906)	2.08 (± 9.196)
Change at C17 D1(n=50,23,64,14,58,64)	0.27 (± 7.775)	-1.66 (± 6.681)	0.70 (± 6.071)	2.45 (± 9.012)
Change at C19 D1(n=51,20,26,9,47,60)	-0.59 (± 7.257)	-2.80 (± 6.172)	0.23 (± 9.094)	1.23 (± 10.618)
Change at C21 D1(n=39,15,12,1,33,40)	-0.69 (± 6.947)	-2.59 (± 6.528)	-3.33 (± 6.399)	2.58 (± 8.218)
Change at C23 D1(n=34,12,0,0,22,34)	-1.67 (± 7.003)	-1.38 (± 6.818)	-0.17 (± 4.687)	99999 (± 99999)
Change at C25 D1(n=25,7,0,0,18,25)	-1.83 (± 6.205)	-1.00 (± 6.880)	-0.14 (± 5.305)	99999 (± 99999)
Change at EOT visit(n=8,7,6,5,2,13)	18.50 (± 23.335)	-5.18 (± 11.458)	-2.31 (± 4.715)	6.58 (± 7.197)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	83	260		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=177,159,234,83,165,260)	51.13 (± 9.567)	52.24 (± 8.679)		
Change at C3 D1 (n=148,128,212,67,141,215)	-2.16 (± 9.700)	-3.14 (± 8.654)		
Change at C5 D1 (n=132,106,200,60,128,192)	-0.60 (± 7.948)	-2.78 (± 7.814)		
Change at C7 D1 (n=109,84,177,52,120,161)	-3.14 (± 9.559)	-3.08 (± 7.670)		
Change at C9 D1 (n=79,63,161,41,103,120)	-1.83 (± 7.323)	-2.39 (± 6.782)		
Change at C11 D1(n=72,46,143,31,87,103)	-2.41 (± 7.653)	-3.29 (± 6.800)		

Change at C13 D1(n=65,39,126,26,77,91)	-3.31 (± 7.902)	-2.88 (± 7.359)		
Change at C15 D1(n=56,29,95,18,68,74)	-4.14 (± 5.662)	-2.88 (± 6.566)		
Change at C17 D1(n=50,23,64,14,58,64)	-2.64 (± 9.724)	-1.88 (± 7.375)		
Change at C19 D1(n=51,20,26,9,47,60)	0.00 (± 11.467)	-2.38 (± 7.150)		
Change at C21 D1(n=39,15,12,1,33,40)	-2.00 (± 99999)	-2.58 (± 6.445)		
Change at C23 D1(n=34,12,0,0,22,34)	99999 (± 99999)	-1.38 (± 6.818)		
Change at C25 D1(n=25,7,0,0,18,25)	99999 (± 99999)	-1.00 (± 6.880)		
Change at EOT visit(n=8,7,6,5,2,13)	-1.61 (± 9.115)	-3.81 (± 10.370)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Change From Baseline in EuroQoL-5 Dimension-5 Level (EQ-5D-5L) Index Score at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point title	Part 1 and Part 2: Change From Baseline in EuroQoL-5 Dimension-5 Level (EQ-5D-5L) Index Score at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point description:

EQ-5D-5L is standardized subject completed questionnaire that measures health status in terms of single index value/utility score. It consisted of 2components: health state profile(descriptive system)&visual analogue scale(VAS) in which subjectS rate their overall health status from 0(worst imaginable)-100(best imaginable), higher scores=better health status. EQ-5D health state profile comprises of 5dimensions: mobility,self-care,usual activities,pain/discomfort&anxiety/depression. Each dimension has 5response levels:1=no,2=slight, 3=moderate,4=severe&5=extreme problems. EQ-5D-5L health status index score range between 0-1. Higher score=better health status. FAS included all randomized subjects. Number of subjects analyzed=number of subjects evaluable for this endpoint. n=subjects with available data for each specified category. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1&Part 2 for LGX818

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and end of treatment visit (within14 days after the last dose of study drug)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	167	181	161	235
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181,161,235,83,167,264)	0.74 (± 0.210)	0.76 (± 0.181)	0.73 (± 0.222)	0.75 (± 0.219)

Change at C3 D1 (n=157,143,224,67,153,224)	0.05 (± 0.194)	-0.10 (± 0.199)	0.00 (± 0.196)	0.06 (± 0.204)
Change at C5 D1(n=139,116,206,59,136,198)	0.04 (± 0.196)	-0.15 (± 0.220)	-0.04 (± 0.196)	0.07 (± 0.218)
Change at C7 D1 (n=116,88,187,53,125,169)	0.05 (± 0.201)	-0.13 (± 0.189)	-0.03 (± 0.215)	0.06 (± 0.237)
Change at C9 D1 (n=87,68,163,43,114,130)	0.03 (± 0.237)	-0.15 (± 0.197)	-0.04 (± 0.237)	0.07 (± 0.192)
Change at C11 D1 (n=72,50,144,33,95,105)	0.04 (± 0.197)	-0.18 (± 0.206)	-0.01 (± 0.238)	0.06 (± 0.195)
Change at C13 D1 (n=63,40,130,27,79,90)	0.05 (± 0.225)	-0.17 (± 0.206)	-0.02 (± 0.263)	0.05 (± 0.254)
Change at C15 D1 (n=61,29,101,17,69,78)	0.05 (± 0.208)	-0.18 (± 0.203)	-0.07 (± 0.280)	0.05 (± 0.259)
Change at C17 D1 (n=56,25,66,12,60,68)	0.07 (± 0.193)	-0.14 (± 0.165)	-0.02 (± 0.173)	0.06 (± 0.188)
Change at C19 D1 (n=51,22,28,9,49,60)	0.03 (± 0.239)	-0.18 (± 0.235)	-0.02 (± 0.214)	0.05 (± 0.231)
Change at C21 D1 (n=42,16,12,1,35,43)	0.07 (± 0.132)	-0.14 (± 0.198)	-0.04 (± 0.159)	0.12 (± 0.174)
Change at C23 D1 (n=33,11,0,0,24,33)	0.04 (± 0.139)	-0.11 (± 0.147)	-0.05 (± 0.171)	99999 (± 99999)
Change at C25 D1 (n=26,5,0,0,16,26)	0.07 (± 0.135)	-0.11 (± 0.207)	-0.17 (± 0.221)	99999 (± 99999)
Change at EOT visit (n=5,3,5,4,3,9)	0.03 (± 0.081)	-0.09 (± 0.347)	-0.14 (± 0.103)	-0.27 (± 0.481)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	83	264		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181,161,235,83,167,264)	0.73 (± 0.244)	0.75 (± 0.203)		
Change at C3 D1 (n=157,143,224,67,153,224)	-0.06 (± 0.246)	-0.09 (± 0.214)		
Change at C5 D1(n=139,116,206,59,136,198)	-0.06 (± 0.231)	-0.13 (± 0.227)		
Change at C7 D1 (n=116,88,187,53,125,169)	-0.16 (± 0.220)	-0.14 (± 0.199)		
Change at C9 D1 (n=87,68,163,43,114,130)	-0.11 (± 0.202)	-0.14 (± 0.199)		
Change at C11 D1 (n=72,50,144,33,95,105)	-0.16 (± 0.230)	-0.17 (± 0.213)		
Change at C13 D1 (n=63,40,130,27,79,90)	-0.20 (± 0.216)	-0.18 (± 0.208)		
Change at C15 D1 (n=61,29,101,17,69,78)	-0.26 (± 0.262)	-0.20 (± 0.218)		
Change at C17 D1 (n=56,25,66,12,60,68)	-0.20 (± 0.332)	-0.15 (± 0.203)		
Change at C19 D1 (n=51,22,28,9,49,60)	-0.11 (± 0.328)	-0.17 (± 0.249)		
Change at C21 D1 (n=42,16,12,1,35,43)	-0.11 (± 99999)	-0.14 (± 0.196)		
Change at C23 D1 (n=33,11,0,0,24,33)	99999 (± 99999)	-0.11 (± 0.147)		

Change at C25 D1 (n=26,5,0,0,16,26)	99999 (± 99999)	-0.11 (± 0.207)		
Change at EOT visit (n=5,3,5,4,3,9)	-0.06 (± 0.061)	-0.08 (± 0.249)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Change From Baseline in Global Health Status Score of EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point title	Part 1 and Part 2: Change From Baseline in Global Health Status Score of EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point description:

EORTC QLQ-C30 contains 30items, is composed of multi & single-item measures. These include 5functional scales (physical,role,emotional,cognitive&social functioning), 3symptom scales(fatigue, nausea/vomiting&pain), 6single items (dyspnea,insomnia,appetite loss,constipation,diarrhea&financial impact)&global health status/QOL scale. Employs 28-four point Likert scales with responses: "not at all" to "very much" & two 7-point Likert scales for global health & overall QOL. Responses to all items converted to 0-100 scale. For functional & global QOL scales, higher scores=better level of functioning/QOL. For symptom-oriented scales, higher score=more severe symptoms. Number of subjects analyzed=number of subjects evaluable for this endpoint. FAS included all randomized subjects. n= subjects with available data for each specified category. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1&Part 2 for LGX818 300mg arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and end of treatment visit (within14 days after the last dose of study drug)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	166	181	160	231
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181,160,231,81,166,262)	66.72 (± 21.585)	66.07 (± 21.890)	64.74 (± 23.611)	65.95 (± 23.028)
Change at C3 D1 (n=156,135,220,69,152,225)	3.56 (± 22.463)	-7.64 (± 21.564)	-3.46 (± 25.235)	4.47 (± 23.031)
Change at C5 D1 (n=138,111,205,60,134,198)	1.55 (± 23.441)	-9.24 (± 21.611)	-4.05 (± 23.700)	5.61 (± 19.396)
Change at C7 D1 (n=114,85,188,53,125,167)	1.53 (± 23.220)	-9.21 (± 23.528)	-3.04 (± 28.197)	5.01 (± 24.000)
Change at C9 D1 (n=88,66,157,42,107,130)	-0.55 (± 25.500)	-12.03 (± 19.771)	-6.94 (± 21.512)	4.94 (± 20.258)
Change at C11 D1 (n=71,46,147,31,93,102)	0.81 (± 21.670)	-11.27 (± 20.611)	-3.80 (± 22.202)	4.76 (± 21.212)

Change at C13 D1 (n=64,37,126,26,79,90)	0.42 (± 22.642)	-8.59 (± 22.516)	-2.93 (± 20.621)	5.89 (± 23.642)
Change at C15 D1 (n=58,29,101,17,68,75)	5.02 (± 19.108)	-9.91 (± 23.490)	-10.34 (± 29.852)	6.11 (± 21.695)
Change at C17 D1 (n=55,24,64,14,61,69)	0.41 (± 21.807)	-8.03 (± 17.784)	-6.94 (± 20.214)	5.86 (± 21.806)
Change at C19 D1 (n=50,22,27,9,49,59)	-0.51 (± 17.547)	-9.33 (± 19.169)	-1.89 (± 20.401)	1.23 (± 18.155)
Change at C21 D1 (n=43,16,11,1,34,44)	0.74 (± 16.838)	-11.05 (± 21.725)	-8.85 (± 11.968)	3.03 (± 19.816)
Change at C23 D1 (n=34,12,0,0,24,34)	-1.39 (± 13.157)	-5.64 (± 19.754)	-3.47 (± 18.278)	99999 (± 99999)
Change at C25 D1 (n=26,7,0,0,17,26)	1.96 (± 13.349)	-7.05 (± 18.057)	-2.38 (± 19.670)	99999 (± 99999)
Change at EOT visit (n=7,4,4,2,2,9)	0.00 (± 11.785)	4.76 (± 28.810)	-4.17 (± 10.758)	-6.25 (± 18.478)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	81	262		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181,160,231,81,166,262)	67.39 (± 22.095)	66.48 (± 21.920)		
Change at C3 D1 (n=156,135,220,69,152,225)	-4.95 (± 20.378)	-6.81 (± 21.199)		
Change at C5 D1 (n=138,111,205,60,134,198)	-4.72 (± 22.776)	-7.87 (± 22.011)		
Change at C7 D1 (n=114,85,188,53,125,167)	-7.08 (± 20.955)	-8.53 (± 22.701)		
Change at C9 D1 (n=88,66,157,42,107,130)	-8.73 (± 18.945)	-10.96 (± 19.496)		
Change at C11 D1 (n=71,46,147,31,93,102)	-7.53 (± 19.288)	-10.13 (± 20.197)		
Change at C13 D1 (n=64,37,126,26,79,90)	-9.29 (± 24.645)	-8.80 (± 23.013)		
Change at C15 D1 (n=58,29,101,17,68,75)	-12.75 (± 21.270)	-10.56 (± 22.897)		
Change at C17 D1 (n=55,24,64,14,61,69)	-7.14 (± 20.111)	-7.85 (± 18.127)		
Change at C19 D1 (n=50,22,27,9,49,59)	-0.93 (± 12.805)	-8.05 (± 18.503)		
Change at C21 D1 (n=43,16,11,1,34,44)	0.00 (± 99999)	-10.80 (± 21.535)		
Change at C23 D1 (n=34,12,0,0,24,34)	99999 (± 99999)	-5.64 (± 19.754)		
Change at C25 D1 (n=26,7,0,0,17,26)	99999 (± 99999)	-7.05 (± 18.057)		
Change at EOT visit (n=7,4,4,2,2,9)	4.17 (± 29.463)	4.63 (± 27.039)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Change From Baseline in Emotional Functioning Scale Score of the EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point title	Part 1 and Part 2: Change From Baseline in Emotional Functioning Scale Score of the EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point description:

EORTC QLQ-C30 contains 30items, is composed of multi & single-item measures. These include 5functional scales (physical,role,emotional,cognitive&social functioning), 3symptom scales(fatigue, nausea/vomiting&pain), 6single items (dyspnea,insomnia,appetite loss,constipation,diarrhea&financial impact)&global health status/QOL scale. Employs 28-four point Likert scales with responses: "not at all" to "very much" & two 7-point Likert scales for global health & overall QOL. Responses to all items converted to 0-100 scale. For functional & global QOL scales, higher scores=better level of functioning/QOL. For symptom-oriented scales, higher score=more severe symptoms. Number of subjects analyzed=number of subjects evaluable for this endpoint. FAS included all randomized subjects. n= subjects with available data for each specified category. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1&Part 2 for LGX818 300mg arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and end of treatment visit (within14 days after the last dose of study drug)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	166	181	160	231
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181,160,231,83,166,264)	74.68 (± 21.233)	74.46 (± 22.367)	72.31 (± 24.695)	73.04 (± 24.450)
Change at C3 D1 (n=156,136,220,70,152,226)	3.23 (± 20.588)	-0.34 (± 22.138)	1.88 (± 20.610)	7.29 (± 20.011)
Change at C5 D1 (n=139,111,205,62,134,201)	5.37 (± 19.243)	1.54 (± 22.418)	2.03 (± 20.662)	6.15 (± 21.401)
Change at C7 D1 (n=115,85,188,53,125,168)	5.42 (± 20.027)	0.34 (± 23.104)	2.71 (± 20.875)	9.37 (± 21.088)
Change at C9 D1 (n=88,67,157,42,107,130)	4.47 (± 24.341)	2.15 (± 19.735)	-0.17 (± 24.283)	9.22 (± 21.940)
Change at C11 D1 (n=71,46,147,31,93,102)	4.81 (± 22.102)	0.12 (± 22.205)	4.53 (± 18.148)	10.56 (± 20.850)
Change at C13 D1 (n=64,37,126,26,79,90)	3.52 (± 23.715)	3.78 (± 19.694)	-2.25 (± 22.192)	8.66 (± 21.894)
Change at C15 D1 (n=58,29,101,17,68,75)	7.35 (± 21.813)	2.30 (± 20.755)	-5.46 (± 26.190)	10.59 (± 19.609)
Change at C17 D1 (n=55,24,64,14,61,69)	5.33 (± 20.584)	3.64 (± 21.502)	-1.39 (± 15.862)	10.33 (± 20.415)
Change at C19 D1 (n=50,22,27,9,49,59)	4.25 (± 19.552)	1.00 (± 24.493)	0.38 (± 16.158)	8.33 (± 22.997)
Change at C21 D1 (n=43,16,11,1,34,44)	4.17 (± 19.811)	-1.16 (± 23.751)	-3.13 (± 16.908)	13.13 (± 15.619)

Change at C23 D1 (n=34,12,0,0,24,34)	-1.74 (± 21.420)	2.94 (± 22.556)	-0.69 (± 23.693)	99999 (± 99999)
Change at C25 D1 (n=26,7,0,0,17,26)	3.92 (± 11.456)	-0.32 (± 24.093)	-1.19 (± 34.503)	99999 (± 99999)
Change at EOT visit (n=7,4,4,3,2,10)	41.67 (± 11.785)	-3.57 (± 25.394)	12.50 (± 28.464)	-4.17 (± 14.434)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	83	264		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181,160,231,83,166,264)	74.20 (± 21.488)	74.38 (± 22.054)		
Change at C3 D1 (n=156,136,220,70,152,226)	1.79 (± 19.958)	0.32 (± 21.465)		
Change at C5 D1 (n=139,111,205,62,134,201)	2.96 (± 20.473)	1.98 (± 21.796)		
Change at C7 D1 (n=115,85,188,53,125,168)	-3.62 (± 19.441)	-0.91 (± 22.033)		
Change at C9 D1 (n=88,67,157,42,107,130)	-0.60 (± 16.296)	1.26 (± 18.674)		
Change at C11 D1 (n=71,46,147,31,93,102)	-2.69 (± 17.793)	-0.74 (± 20.915)		
Change at C13 D1 (n=64,37,126,26,79,90)	-6.41 (± 17.998)	0.83 (± 19.675)		
Change at C15 D1 (n=58,29,101,17,68,75)	-2.12 (± 13.232)	1.30 (± 19.317)		
Change at C17 D1 (n=55,24,64,14,61,69)	1.79 (± 15.736)	3.26 (± 20.373)		
Change at C19 D1 (n=50,22,27,9,49,59)	2.78 (± 16.667)	1.27 (± 23.357)		
Change at C21 D1 (n=43,16,11,1,34,44)	16.67 (± 99999)	-0.76 (± 23.626)		
Change at C23 D1 (n=34,12,0,0,24,34)	99999 (± 99999)	2.94 (± 22.556)		
Change at C25 D1 (n=26,7,0,0,17,26)	99999 (± 99999)	-0.32 (± 24.093)		
Change at EOT visit (n=7,4,4,3,2,10)	5.56 (± 4.811)	-0.83 (± 21.318)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Change From Baseline in Physical Functioning Scale Score of the EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point title	Part 1 and Part 2: Change From Baseline in Physical Functioning Scale Score of the EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point description:

EORTC QLQ-C30 contains 30items, is composed of multi & single-item measures. These include 5functional scales (physical,role,emotional,cognitive&social functioning), 3symptom scales(fatigue, nausea/vomiting&pain), 6single items (dyspnea,insomnia,appetite loss,constipation,diarrhea&financial impact)&global health status/QOL scale. Employs 28-four point Likert scales with responses: "not at all" to "very much" & two 7-point Likert scales for global health & overall QOL. Responses to all items converted to 0-100 scale. For functional & global QOL scales, higher scores=better level of functioning/QOL. For symptom-oriented scales, higher score=more severe symptoms. Number of subjects analyzed=number of subjects evaluable for this endpoint. FAS included all randomized subjects. n= subjects with available data for each specified category. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1&Part 2 for LGX818 300mg arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and end of treatment visit (within14 days after the last dose of study drug)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	167	180	159	235
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=180,159,235,83,167,263)	82.10 (± 19.593)	83.18 (± 20.266)	80.71 (± 22.182)	80.67 (± 21.889)
Change at C3 D1 (n=157,135,222,70,153,227)	0.20 (± 18.033)	-13.79 (± 20.396)	-2.90 (± 20.319)	2.94 (± 16.831)
Change at C5 D1 (n=138,111,208,62,135,200)	0.15 (± 18.388)	-17.14 (± 22.276)	-7.45 (± 17.792)	2.73 (± 17.748)
Change at C7 D1 (n=115,84,191,53,127,168)	-1.93 (± 18.071)	-16.26 (± 21.719)	-6.98 (± 19.605)	1.22 (± 17.469)
Change at C9 D1 (n=88,66,160,42,110,130)	-0.45 (± 20.511)	-19.43 (± 20.755)	-6.82 (± 21.881)	3.03 (± 16.525)
Change at C11 D1 (n=71,45,148,31,94,102)	-0.85 (± 18.767)	-22.65 (± 20.867)	-4.11 (± 18.680)	0.50 (± 17.734)
Change at C13 D1 (n=64,36,127,26,80,90)	-1.25 (± 19.705)	-20.00 (± 20.874)	-6.30 (± 22.534)	0.47 (± 18.290)
Change at C15 D1 (n=58,30,101,17,69,75)	0.29 (± 17.356)	-20.26 (± 21.030)	-6.22 (± 21.580)	-0.40 (± 22.466)
Change at C17 D1 (n=55,25,66,14,63,69)	-0.03 (± 17.862)	-18.88 (± 20.072)	-3.27 (± 19.817)	-0.88 (± 16.432)
Change at C19 D1 (n=49,21,28,9,49,58)	-1.22 (± 16.140)	-20.07 (± 21.417)	-1.90 (± 20.237)	-5.71 (± 16.301)
Change at C21 D1 (n=43,16,11,1,35,44)	-0.95 (± 13.150)	-16.86 (± 19.694)	-4.90 (± 19.355)	-8.48 (± 23.303)
Change at C23 D1 (n=34,12,0,0,24,34)	-5.00 (± 13.656)	-14.46 (± 18.298)	-2.22 (± 19.557)	99999 (± 99999)
Change at C25 D1 (n=25,7,0,0,17,25)	-5.49 (± 14.575)	-15.93 (± 17.092)	-4.76 (± 23.637)	99999 (± 99999)
Change at EOT visit (n=7,4,4,3,2,10)	33.33 (± 47.140)	-0.95 (± 22.910)	-15.00 (± 19.149)	-5.00 (± 10.000)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	83	263		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=180,159,235,83,167,263)	81.45 (± 21.890)	82.63 (± 20.766)		
Change at C3 D1 (n=157,135,222,70,153,227)	-13.63 (± 22.428)	-13.74 (± 20.994)		
Change at C5 D1 (n=138,111,208,62,135,200)	-12.63 (± 21.570)	-15.74 (± 22.104)		
Change at C7 D1 (n=115,84,191,53,127,168)	-17.01 (± 20.200)	-16.49 (± 21.194)		
Change at C9 D1 (n=88,66,160,42,110,130)	-15.83 (± 16.269)	-18.27 (± 19.429)		
Change at C11 D1 (n=71,45,148,31,94,102)	-13.49 (± 13.665)	-19.87 (± 19.369)		
Change at C13 D1 (n=64,36,127,26,80,90)	-13.85 (± 17.781)	-18.22 (± 20.127)		
Change at C15 D1 (n=58,30,101,17,69,75)	-24.31 (± 22.845)	-21.18 (± 21.364)		
Change at C17 D1 (n=55,25,66,14,63,69)	-19.05 (± 23.367)	-18.91 (± 20.599)		
Change at C19 D1 (n=49,21,28,9,49,58)	-14.07 (± 14.699)	-19.14 (± 20.527)		
Change at C21 D1 (n=43,16,11,1,35,44)	-13.33 (± 99999)	-16.78 (± 19.471)		
Change at C23 D1 (n=34,12,0,0,24,34)	99999 (± 99999)	-14.46 (± 18.298)		
Change at C25 D1 (n=25,7,0,0,17,25)	99999 (± 99999)	-15.93 (± 17.092)		
Change at EOT visit (n=7,4,4,3,2,10)	-4.44 (± 3.849)	-2.00 (± 18.869)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Change From Baseline in Social Functioning Scale Score of the EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point title	Part 1 and Part 2: Change From Baseline in Social Functioning Scale Score of the EORTC QLQ-C30 at Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and End of Treatment Visit

End point description:

EORTC QLQ-C30 contains 30items, is composed of multi & single-item measures. These include 5functional scales (physical,role,emotional,cognitive&social functioning), 3symptom scales(fatigue, nausea/vomiting&pain), 6single items (dyspnea,insomnia,appetite loss,constipation,diarrhea&financial impact)&global health status/QOL scale. Employs 28-four point Likert scales with responses: "not at all" to "very much" & two 7-point Likert scales for global health & overall QOL. Responses to all items converted to 0-100 scale. For functional & global QOL scales, higher scores=better level of functioning/QOL. For symptom-oriented scales, higher score=more severe symptoms. Number of subjects analyzed=number of subjects evaluable for this endpoint. FAS included all randomized subjects. n= subjects with available data for each specified category. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1&Part 2 for LGX818 300mg arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), Day 1 of Cycle 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and end of treatment visit (within14 days after the last dose of study drug)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	179	160	229
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=179,160,229,83,164,262)	80.69 (± 24.696)	80.91 (± 23.841)	78.54 (± 26.854)	81.37 (± 25.262)
Change at C3 D1 (n=155,136,218,70,152,225)	-0.66 (± 27.854)	-10.86 (± 28.967)	-4.90 (± 30.097)	4.05 (± 22.461)
Change at C5 D1 (n=137,111,203,62,133,199)	3.26 (± 27.559)	-11.92 (± 32.145)	-7.21 (± 27.026)	3.37 (± 20.604)
Change at C7 D1 (n=114,85,186,54,124,168)	2.82 (± 28.807)	-9.80 (± 28.979)	-2.75 (± 31.586)	3.05 (± 22.185)
Change at C9 D1 (n=87,67,155,42,106,129)	1.57 (± 31.834)	-15.71 (± 26.579)	-1.99 (± 30.084)	3.66 (± 21.002)
Change at C11 D1 (n=70,46,145,31,92101)	-2.72 (± 29.160)	-12.62 (± 27.428)	-0.36 (± 28.865)	1.95 (± 23.032)
Change at C13 D1 (n=63,37,124,26,78,89)	-4.27 (± 28.228)	-11.38 (± 28.053)	-0.45 (± 27.635)	1.75 (± 24.585)
Change at C15 D1 (n=58,29,99,17,67,75)	3.73 (± 25.921)	-10.63 (± 27.695)	-6.32 (± 34.622)	2.86 (± 22.340)
Change at C17 D1 (n=54,24,63,14,60,68)	1.11 (± 27.251)	-11.42 (± 25.865)	1.39 (± 25.020)	1.59 (± 22.543)
Change at C19 D1 (n=50,22,27,9,48,59)	-1.04 (± 30.248)	-12.33 (± 30.826)	3.79 (± 26.192)	1.23 (± 22.133)
Change at C21 D1 (n=43,16,11,1,33,44	-1.52 (± 32.103)	-14.73 (± 30.257)	-3.13 (± 22.948)	4.55 (± 18.395)
Change at C23 D1 (34,12,0,0,23,34)	-12.32 (± 28.077)	-6.37 (± 20.521)	1.39 (± 15.006)	99999 (± 99999)
Change at C25 D1 (n=26,7,0,0,16,26)	-5.21 (± 23.348)	-7.05 (± 24.117)	4.76 (± 20.893)	99999 (± 99999)
Change at EOT visit (n=7,4,4,3,2,10)	25.00 (± 35.355)	-19.05 (± 26.227)	-8.33 (± 9.623)	-16.67 (± 30.429)

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	83	262		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=179,160,229,83,164,262)	78.31 (± 28.600)	80.09 (± 25.418)		
Change at C3 D1 (n=155,136,218,70,152,225)	-10.00 (± 26.829)	-10.59 (± 28.262)		

Change at C5 D1 (n=137,111,203,62,133,199)	-5.11 (± 28.244)	-9.80 (± 31.073)		
Change at C7 D1 (n=114,85,186,54,124,168)	-13.89 (± 27.992)	-11.11 (± 28.646)		
Change at C9 D1 (n=87,67,155,42,106,129)	-9.52 (± 14.790)	-13.70 (± 23.520)		
Change at C11 D1 (n=70,46,145,31,92101)	-12.37 (± 23.161)	-12.54 (± 26.077)		
Change at C13 D1 (n=63,37,124,26,78,89)	-5.77 (± 18.822)	-9.74 (± 25.723)		
Change at C15 D1 (n=58,29,99,17,67,75)	-15.69 (± 16.106)	-11.78 (± 25.524)		
Change at C17 D1 (n=54,24,63,14,60,68)	-7.14 (± 28.280)	-10.54 (± 26.219)		
Change at C19 D1 (n=50,22,27,9,48,59)	-12.96 (± 34.134)	-12.43 (± 31.041)		
Change at C21 D1 (n=43,16,11,1,33,44	-33.33 (± 99999)	-15.15 (± 30.034)		
Change at C23 D1 (34,12,0,0,23,34)	99999 (± 99999)	-6.37 (± 20.521)		
Change at C25 D1 (n=26,7,0,0,16,26)	99999 (± 99999)	-7.05 (± 24.117)		
Change at EOT visit (n=7,4,4,3,2,10)	0.00 (± 33.333)	-13.33 (± 28.109)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Number of Subjects With Change From Baseline in Eastern Cooperative Oncology Group Performance Status (ECOG PS)

End point title	Part 1 and Part 2: Number of Subjects With Change From Baseline in Eastern Cooperative Oncology Group Performance Status (ECOG PS)

End point description:

ECOG: subject's performance status was measured on a 6-point scale: 0= fully active/able to carry on all pre-disease activities without restriction; 1=restricted in physically strenuous activity but ambulatory and able to carry out work of a light and sedentary nature; 2= ambulatory and capable of all self-care, but unable to carry out any work activities, up and about more than 50% of waking hours; 3= capable of only limited self-care, confined to bed/chair >50% of waking hours; 4= completely disabled, cannot carry on any self-care, totally confined to bed/chair. Safety analysis set. It was planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm. 99999=data could not be estimated due to low number of subjects with events. Number of subjects analyzed=number of subjects evaluable for this endpoint. n= subjects with available data for each specified category. Data is reported only for categories with non-zero values.

End point type	Secondary

End point timeframe:

Part 1 and Part 2: Baseline, Day 1 of each cycle (Cycle 2 to Cycle 119 including 30 days[D] safety follow up [fup]) (each cycle=28 days)

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	192	192	186	257
Units: subjects				
Baseline: ECOG score0 (n=192,186,257,84,192,276)	136	139	135	189
Baseline: ECOG score1 (n=192,186,257,84,192,276)	56	53	51	68
C2 D1: ECOG score 0 (n=182,181,256,80,188,262)	142	98	113	193
C2 D1: ECOG score 1 (n=182,181,256,80,188,262)	44	79	64	62
C2 D1: ECOG score 2 (n=182,181,256,80,188,262)	1	3	4	1
C2 D1: ECOG score 3 (n=182,181,256,80,188,262)	0	2	0	0
C2 D1: ECOG score 4 (n=182,181,256,80,188,262)	1	0	0	0
C3 D1: ECOG score 0 (n=175,176,253,74,185,249)	131	90	107	197
C3 D1: ECOG score 1 (n=175,176,253,74,185,249)	53	81	64	55
C3 D1: ECOG score 2 (n=175,176,253,74,185,249)	1	4	4	1
C4 D1: ECOG score 0 (n=164,158,250,68,179,232)	128	93	98	189
C4 D1: ECOG score 1 (n=164,158,250,68,179,232)	50	66	52	56
C4 D1: ECOG score 2 (n=164,158,250,68,179,232)	1	4	4	4
C4 D1: ECOG score 3 (n=164,158,250,68,179,232)	0	1	4	1
C5 D1: ECOG score 0 (n=158,143,239,66,174,224)	127	85	82	181
C5 D1: ECOG score 1 (n=158,143,239,66,174,224)	43	69	52	55
C5 D1: ECOG score 2 (n=158,143,239,66,174,224)	3	4	7	2
C5 D1: ECOG score 3 (n=158,143,239,66,174,224)	1	0	1	1
C5 D1: ECOG score 4 (n=158,143,239,66,174,224)	0	0	1	0
C6 D1: ECOG score 0 (n=137,126,231,58,169,195)	124	68	78	168
C6 D1: ECOG score 1 (n=137,126,231,58,169,195)	45	65	46	58
C6 D1: ECOG score 2 (n=137,126,231,58,169,195)	0	3	1	3
C6 D1: ECOG score 3 (n=137,126,231,58,169,195)	0	0	1	1
C6 D1: ECOG score 4 (n=137,126,231,58,169,195)	0	1	0	1
C7 D1: ECOG score 0 (n=129,111,218,55,159,184)	112	68	74	158
C7 D1: ECOG score 1 (n=129,111,218,55,159,184)	46	60	35	58
C7 D1: ECOG score 2 (n=129,111,218,55,159,184)	1	1	2	2

C8 D1: ECOG score 0 (n=108,95,200,46,148,154)	112	55	58	140
C8 D1: ECOG score 1 (n=108,95,200,46,148,154)	33	49	33	58
C8 D1: ECOG score 2 (n=108,95,200,46,148,154)	2	3	4	1
C8 D1: ECOG score 3 (n=108,95,200,46,148,154)	1	1	0	1
C9 D1: ECOG score 0 (n=98,90,188,43,144,141)	102	50	55	135
C9 D1: ECOG score 1 (n=98,90,188,43,144,141)	36	47	30	52
C9 D1: ECOG score 2 (n=98,90,188,43,144,141)	4	1	4	0
C9 D1: ECOG score 3 (n=98,90,188,43,144,141)	0	0	1	0
C9 D1: ECOG score 4 (n=98,90,188,43,144,141)	1	0	0	1
C10 D1: ECOG score 0 (n=88,73,171,37,129,125)	94	52	44	121
C10 D1: ECOG score 1 (n=88,73,171,37,129,125)	32	35	26	46
C10 D1: ECOG score 2 (n=88,73,171,37,129,125)	3	1	2	3
C10 D1: ECOG score 3 (n=88,73,171,37,129,125)	0	0	1	1
C11 D1: ECOG score 0 (n=85,62,158,36,121,121)	89	44	39	116
C11 D1: ECOG score 1 (n=85,62,158,36,121,121)	30	40	20	42
C11 D1: ECOG score 2 (n=85,62,158,36,121,121)	2	1	2	0
C11 D1: ECOG score 3 (n=85,62,158,36,121,121)	0	0	1	0
C12 D1: ECOG score 0 (n=77,50,152,30,110,107)	84	44	31	113
C12 D1: ECOG score 1 (n=77,50,152,30,110,107)	25	31	16	38
C12 D1: ECOG score 2 (n=77,50,152,30,110,107)	1	1	2	0
C12 D1: ECOG score 3 (n=77,50,152,30,110,107)	0	1	1	0
C12 D1: ECOG score 4 (n=77,50,152,30,110,107)	0	0	0	1
C13 D1: ECOG score 0 (n=73,47,143,31,100,104)	77	41	27	102
C13 D1: ECOG score 1 (n=73,47,143,31,100,104)	22	31	18	39
C13 D1: ECOG score 2 (n=73,47,143,31,100,104)	1	1	2	1
C13 D1: ECOG score 4 (n=73,47,143,31,100,104)	0	0	0	1
C14 D1: ECOG score 0 (n=75,46,136,27,97,102)	74	47	25	100
C14 D1: ECOG score 1 (n=75,46,136,27,97,102)	23	27	19	33
C14 D1: ECOG score 2 (n=75,46,136,27,97,102)	0	0	2	2
C14 D1: ECOG score 3 (n=75,46,136,27,97,102)	0	0	0	1
C14 D1: ECOG score 4 (n=75,46,136,27,97,102)	0	1	0	0

C15 D1: ECOG score 0 (n=72,41,126,25,94,97)	72	41	22	93
C15 D1: ECOG score 1 (n=72,41,126,25,94,97)	20	30	18	31
C15 D1: ECOG score 2 (n=72,41,126,25,94,97)	1	1	1	1
C15 D1: ECOG score 3 (n=72,41,126,25,94,97)	1	0	0	0
C15 D1: ECOG score 4 (n=72,41,126,25,94,97)	0	0	0	1
C16 D1: ECOG score 0 (n=67,35,116,24,90,91)	65	41	24	82
C16 D1: ECOG score 1 (n=67,35,116,24,90,91)	24	23	10	33
C16 D1: ECOG score 2 (n=67,35,116,24,90,91)	1	3	1	0
C16 D1: ECOG score 3 (n=67,35,116,24,90,91)	0	0	0	1
C17 D1: ECOG score 0 (n=67,33,111,23,86,90)	68	39	21	80
C17 D1: ECOG score 1 (n=67,33,111,23,86,90)	17	27	11	30
C17 D1: ECOG score 2 (n=67,33,111,23,86,90)	1	1	1	1
C18 D1: ECOG score 0 (n=60,33,104,23,85,83)	68	36	18	75
C18 D1: ECOG score 1 (n=60,33,104,23,85,83)	16	24	13	28
C18 D1: ECOG score 2 (n=60,33,104,23,85,83)	1	0	1	1
C18 D1: ECOG score 3 (n=60,33,104,23,85,83)	0	0	1	0
C19 D1: ECOG score 0 (n=59,34,98,22,80,81)	66	38	21	70
C19 D1: ECOG score 1 (n=59,34,98,22,80,81)	12	20	11	26
C19 D1: ECOG score 2 (n=59,34,98,22,80,81)	2	1	2	1
C20 D1: ECOG score 0 (n=52,32,94,23,80,75)	70	31	20	68
C20 D1: ECOG score 1 (n=52,32,94,23,80,75)	9	19	11	25
C20 D1: ECOG score 2 (n=52,32,94,23,80,75)	0	2	1	0
C20 D1: ECOG score 3 (n=52,32,94,23,80,75)	1	0	0	1
C21 D1: ECOG score 0 (n=49,29,92,23,75,72)	62	29	17	69
C21 D1: ECOG score 1 (n=49,29,92,23,75,72)	13	19	11	23
C21 D1: ECOG score 2 (n=49,29,92,23,75,72)	0	1	1	0
C22 D1: ECOG score 0 (n=46,27,86,21,72,67)	60	28	17	63
C22 D1: ECOG score 1 (n=46,27,86,21,72,67)	12	16	9	22
C22 D1: ECOG score 3 (n=46,27,86,21,72,67)	0	1	0	0
C22 D1: ECOG score 4 (n=46,27,86,21,72,67)	0	1	0	0
C23 D1: ECOG score 0 (n=40,26,81,19,67,59)	56	28	16	60

C23 D1: ECOG score 1 (n=40,26,81,19,67,59)	10	12	7	20
C23 D1: ECOG score 2 (n=40,26,81,19,67,59)	1	0	3	1
C24 D1: ECOG score 0 (n=38,27,80,19,68,57)	55	28	15	61
C24 D1: ECOG score 1 (n=38,27,80,19,68,57)	13	10	11	19
C24 D1: ECOG score 2 (n=38,27,80,19,68,57)	0	0	1	0
C25 D1: ECOG score 0 (n=38,25,80,19,64,57)	55	28	17	60
C25 D1: ECOG score 1 (n=38,25,80,19,64,57)	8	10	8	20
C25 D1: ECOG score 2 (n=38,25,80,19,64,57)	1	0	0	0
C26 D1: ECOG score 0 (n=37,25,80,19,61,56)	51	27	16	60
C26 D1: ECOG score 1 (n=37,25,80,19,61,56)	9	10	8	20
C26 D1: ECOG score 2 (n=37,25,80,19,61,56)	1	0	1	0
C27 D1: ECOG score 0 (n=36,23,76,19,58,55)	48	28	13	57
C27 D1: ECOG score 1 (n=36,23,76,19,58,55)	9	8	9	18
C27 D1: ECOG score 2 (n=36,23,76,19,58,55)	1	0	1	1
C28 D1: ECOG score 0 (n=34,22,70,18,56,52)	50	25	14	52
C28 D1: ECOG score 1 (n=34,22,70,18,56,52)	6	9	7	18
C28 D1: ECOG score 2 (n=34,22,70,18,56,52)	0	0	1	0
C29 D1: ECOG score 0 (n=34,21,67,16,56,50)	45	22	13	51
C29 D1: ECOG score 1 (n=34,21,67,16,56,50)	10	12	8	16
C29 D1: ECOG score 2 (n=34,21,67,16,56,50)	0	0	0	0
C29 D1: ECOG score 3 (n=34,21,67,16,56,50)	1	0	0	0
C30 D1: ECOG score 0 (n=32,21,69,15,55,47)	55	23	13	50
C30 D1: ECOG score 1 (n=32,21,69,15,55,47)	40	9	8	18
C30 D1: ECOG score 2 (n=32,21,69,15,55,47)	0	0	0	1
C30 D1: ECOG score 4 (n=32,21,69,15,55,47)	1	0	0	0
C31 D1: ECOG score 0 (n=32,21,62,15,55,47)	45	24	12	48
C31 D1: ECOG score 1 (n=32,21,62,15,55,47)	8	8	9	13
C31 D1: ECOG score 2 (n=32,21,62,15,55,47)	1	0	0	1
C31 D1: ECOG score 4 (n=32,21,62,15,55,47)	1	0	0	0
C32 D1: ECOG score 0 (n=30,20,63,14,52,44)	43	21	12	49
C32 D1: ECOG score 1 (n=30,20,63,14,52,44)	9	8	8	14

C32 D1: ECOG score 2 (n=30,20,63,14,52,44)	0	1	0	0
C33 D1: ECOG score 0 (n=27,20,61,15,52,42)	47	21	14	47
C33 D1: ECOG score 1 (n=27,20,61,15,52,42)	5	6	6	13
C33 D1: ECOG score 2 (n=27,20,61,15,52,42)	0	0	0	1
C34 D1: ECOG score 0 (n=26,19,61,15,52,41)	46	18	13	47
C34 D1: ECOG score 1 (n=26,19,61,15,52,41)	6	8	6	13
C34 D1: ECOG score 2 (n=26,19,61,15,52,41)	0	0	0	1
C35 D1: ECOG score 0 (n=27,19,61,15,52,42)	42	19	13	45
C35 D1: ECOG score 1 (n=27,19,61,15,52,42)	10	7	6	15
C35 D1: ECOG score 2 (n=27,19,61,15,52,42)	0	0	0	1
C36 D1: ECOG score 0 (n=25,18,60,15,51,40)	45	20	12	44
C36 D1: ECOG score 1 (n=25,18,60,15,51,40)	6	5	6	15
C36 D1: ECOG score 2 (n=25,18,60,15,51,40)	0	0	0	1
C37 D1: ECOG score 0 (n=25,17,58,14,47,39)	39	18	9	43
C37 D1: ECOG score 1 (n=25,17,58,14,47,39)	8	7	8	15
C37 D1: ECOG score 2 (n=25,17,58,14,47,39)	0	0	0	0
C38 D1: ECOG score 0 (n=25,17,59,13,48,38)	42	17	10	43
C38 D1: ECOG score 1 (n=25,17,59,13,48,38)	5	8	7	15
C38 D1: ECOG score 2 (n=25,17,59,13,48,38)	0	0	0	1
C38 D1: ECOG score 3 (n=25,17,59,13,48,38)	1	0	0	0
C39 D1: ECOG score 0 (n=25,16,57,14,47,39)	40	20	9	42
C39 D1: ECOG score 1 (n=25,16,57,14,47,39)	6	5	7	14
C39 D1: ECOG score 2 (n=25,16,57,14,47,39)	1	0	0	1
C40 D1: ECOG score 0 (n=24,16,55,12,45,36)	38	17	10	40
C40 D1: ECOG score 1 (n=24,16,55,12,45,36)	6	7	6	14
C40 D1: ECOG score 2 (n=24,16,55,12,45,36)	1	0	0	1
C41 D1: ECOG score 0 (n=23,15,56,13,44,36)	37	17	7	41
C41 D1: ECOG score 1 (n=23,15,56,13,44,36)	7	6	7	15
C41 D1: ECOG score 2 (n=23,15,56,13,44,36)	0	0	1	0
C42 D1: ECOG score 0 (n=23,14,55,13,41,36)	38	18	8	40
C42 D1: ECOG score 1 (n=23,14,55,13,41,36)	3	5	6	15

C42 D1: ECOG score 2 (n=23,14,55,13,41,36)	0	0	0	0
C43 D1: ECOG score 0 (n=23,14,54,13,39,36)	35	18	8	39
C43 D1: ECOG score 1 (n=23,14,54,13,39,36)	4	5	6	15
C43 D1: ECOG score 2 (n=23,14,54,13,39,36)	0	0	0	0
C44 D1: ECOG score 0 (n=23,14,54,13,41,36)	38	17	7	39
C44 D1: ECOG score 1 (n=23,14,54,13,41,36)	3	6	7	15
C44 D1: ECOG score 2 (n=23,14,54,13,41,36)	0	0	0	0
C45 D1: ECOG score 0 (n=23,14,52,10,40,33)	37	17	8	35
C45 D1: ECOG score 1 (n=23,14,52,10,40,33)	3	6	6	17
C46 D1: ECOG score 0 (n=21,11,49,10,40,31)	34	17	6	37
C46 D1: ECOG score 1 (n=21,11,49,10,40,31)	6	4	5	12
C47 D1: ECOG score 0 (n=23,10,49,10,40,33)	32	18	5	36
C47 D1: ECOG score 1 (n=23,10,49,10,40,33)	8	5	5	13
C48 D1: ECOG score 0 (n=22,11,50,9,38,31)	34	17	6	36
C48 D1: ECOG score 1 (n=22,11,50,9,38,31)	4	5	5	13
C48 D1: ECOG score 3 (n=22,11,50,9,38,31)	0	0	0	1
C49 D1: ECOG score 0 (n=21,10,47,9,38,30)	35	14	6	35
C49 D1: ECOG score 1 (n=21,10,47,9,38,30)	3	7	4	9
C49 D1: ECOG score 2 (n=21,10,47,9,38,30)	0	0	0	2
C49 D1: ECOG score 3 (n=21,10,47,9,38,30)	0	0	0	1
C50 D1: ECOG score 0 (n=21,10,46,8,39,29)	36	16	5	35
C50 D1: ECOG score 1 (n=21,10,46,8,39,29)	3	5	5	10
C50 D1: ECOG score 2 (n=21,10,46,8,39,29)	0	0	0	1
C51 D1: ECOG score 0 (n=19,10,43,8,38,27)	34	16	5	29
C51 D1: ECOG score 1 (n=19,10,43,8,38,27)	4	3	5	13
C51 D1: ECOG score 2 (n=19,10,43,8,38,27)	0	0	0	1
C52 D1: ECOG score 0 (n=20,10,44,8,38,28)	32	14	5	31
C52 D1: ECOG score 1 (n=20,10,44,8,38,28)	6	6	5	12
C52 D1: ECOG score 2 (n=20,10,44,8,38,28)	0	0	0	1
C53 D1: ECOG score 0 (n=20,10,42,7,37,27)	32	14	5	32
C53 D1: ECOG score 1 (n=20,10,42,7,37,27)	5	6	5	9

C53 D1: ECOG score 2 (n=20,10,42,7,37,27)	0	0	0	1
C54 D1: ECOG score 0 (n=20,10,42,8,33,28)	26	14	5	30
C54 D1: ECOG score 1 (n=20,10,42,8,33,28)	7	6	5	11
C54 D1: ECOG score 2 (n=20,10,42,8,33,28)	0	0	0	1
C55 D1: ECOG score 0 (n=20,10,41,7,36,27)	30	15	5	30
C55 D1: ECOG score 1 (n=20,10,41,7,36,27)	6	5	5	10
C55 D1: ECOG score 2 (n=20,10,41,7,36,27)	0	0	0	1
C56 D1: ECOG score 0 (n=20,9,40,7,36,27)	29	13	4	29
C56 D1: ECOG score 1 (n=20,9,40,7,36,27)	7	7	5	10
C56 D1: ECOG score 2 (n=20,9,40,7,36,27)	0	0	0	1
C57 D1: ECOG score 0 (n=19,8,39,7,35,26)	27	15	3	29
C57 D1: ECOG score 1 (n=19,8,39,7,35,26)	8	4	5	9
C57 D1: ECOG score 2 (n=19,8,39,7,35,26)	0	0	0	1
C58 D1: ECOG score 0 (n=19,10,37,7,34,26)	29	14	6	26
C58 D1: ECOG score 1 (n=19,10,37,7,34,26)	5	5	4	10
C58 D1: ECOG score 2 (n=19,10,37,7,34,26)	0	0	0	1
C59 D1: ECOG score 0 (n=18,8,36,6,33,24)	27	13	6	25
C59 D1: ECOG score 1 (n=18,8,36,6,33,24)	6	5	2	10
C59 D1: ECOG score 2 (n=18,8,36,6,33,24)	0	0	0	1
C60 D1: ECOG score 0 (n=17,8,38,5,32,22)	28	13	5	26
C60 D1: ECOG score 1 (n=17,8,38,5,32,22)	3	4	3	11
C60 D1: ECOG score 2 (n=17,8,38,5,32,22)	1	0	0	1
C61 D1: ECOG score 0 (n=18,8,35,5,30,23)	26	13	5	24
C61 D1: ECOG score 1 (n=18,8,35,5,30,23)	4	5	2	10
C61 D1: ECOG score 2 (n=18,8,35,5,30,23)	0	0	0	1
C61 D1: ECOG score 3 (n=18,8,35,5,30,23)	0	0	1	0
C62 D1: ECOG score 0 (n=17,7,35,5,29,22)	24	13	5	24
C62 D1: ECOG score 1 (n=17,7,35,5,29,22)	5	4	2	10
C62 D1: ECOG score 2 (n=17,7,35,5,29,22)	0	0	0	1
C63 D1: ECOG score 0 (n=17,7,33,5,28,22)	22	13	5	24
C63 D1: ECOG score 1 (n=17,7,33,5,28,22)	6	4	2	8

C63 D1: ECOG score 2 (n=17,7,33,5,28,22)	0	0	0	1
C64 D1: ECOG score 0 (n=17,7,32,5,28,22)	23	11	5	25
C64 D1: ECOG score 1 (n=17,7,32,5,28,22)	5	6	2	6
C64 D1: ECOG score 2 (n=17,7,32,5,28,22)	0	0	0	1
C65 D1: ECOG score 0 (n=16,7,29,4,28,20)	21	13	5	18
C65 D1: ECOG score 1 (n=16,7,29,4,28,20)	7	3	2	10
C65 D1: ECOG score 2 (n=16,7,29,4,28,20)	0	0	0	1
C66 D1: ECOG score 0 (n=17,7,32,4,28,21)	24	12	5	21
C66 D1: ECOG score 1 (n=17,7,32,4,28,21)	4	5	2	10
C66 D1: ECOG score 2 (n=17,7,32,4,28,21)	0	0	0	1
C67 D1: ECOG score 0 (n=15,7,29,5,28,20)	24	13	5	19
C67 D1: ECOG score 1 (n=15,7,29,5,28,20)	4	2	2	9
C67 D1: ECOG score 2 (n=15,7,29,5,28,20)	0	0	0	1
C68 D1: ECOG score 0 (n=15,6,29,5,28,20)	24	13	4	19
C68 D1: ECOG score 1 (n=15,6,29,5,28,20)	4	2	2	9
C68 D1: ECOG score 2 (n=15,6,29,5,28,20)	0	0	0	1
C69 D1: ECOG score 0 (n=14,6,30,5,26,19)	21	12	5	20
C69 D1: ECOG score 1 (n=14,6,30,5,26,19)	5	2	1	9
C69 D1: ECOG score 2 (n=14,6,30,5,26,19)	0	0	0	1
C70 D1: ECOG score 0 (n=14,6,29,5,27,19)	22	11	4	20
C70 D1: ECOG score 1 (n=14,6,29,5,27,19)	5	3	2	8
C70 D1: ECOG score 2 (n=14,6,29,5,27,19)	0	0	0	1
C71 D1: ECOG score 0 (n=14,6,24,4,26,18)	21	12	4	15
C71 D1: ECOG score 1 (n=14,6,24,4,26,18)	5	2	2	8
C71 D1: ECOG score 2 (n=14,6,24,4,26,18)	0	0	0	1
C72 D1: ECOG score 0 (n=14,5,32,4,28,18)	23	11	4	21
C72 D1: ECOG score 1 (n=14,5,32,4,28,18)	5	3	1	10
C72 D1: ECOG score 2 (n=14,5,32,4,28,18)	0	0	0	1
C73 D1: ECOG score 0 (n=13,5,24,4,25,17)	24	12	4	15
C73 D1: ECOG score 1 (n=13,5,24,4,25,17)	1	1	1	8
C73 D1: ECOG score 2 (n=13,5,24,4,25,17)	0	0	0	1

C74 D1: ECOG score 0 (n=14,5,25,5,26,19)	22	13	3	16
C74 D1: ECOG score 1 (n=14,5,25,5,26,19)	4	1	2	8
C74 D1: ECOG score 2 (n=14,5,25,5,26,19)	0	0	0	1
C75 D1: ECOG score 0 (n=13,5,29,3,25,16)	22	12	3	21
C75 D1: ECOG score 1 (n=13,5,29,3,25,16)	2	1	2	8
C75 D1: ECOG score 2 (n=13,5,29,3,25,16)	1	0	0	0
C76 D1: ECOG score 0 (n=14,3,24,4,24,18)	21	13	2	17
C76 D1: ECOG score 1 (n=14,3,24,4,24,18)	2	1	1	6
C76 D1: ECOG score 2 (n=14,3,24,4,24,18)	1	0	0	1
C77 D1: ECOG score 0 (n=12,3,21,4,20,16)	18	11	2	13
C77 D1: ECOG score 1 (n=12,3,21,4,20,16)	2	1	1	8
C78 D1: ECOG score 0 (n=13,3,31,2,19,15)	17	12	2	21
C78 D1: ECOG score 1 (n=13,3,31,2,19,15)	2	1	1	9
C78 D1: ECOG score 2 (n=13,3,31,2,19,15)	0	0	0	1
C79 D1: ECOG score 0 (n=14,2,22,2,21,16)	18	12	1	16
C79 D1: ECOG score 1 (n=14,2,22,2,21,16)	3	2	1	5
C79 D1: ECOG score 2 (n=14,2,22,2,21,16)	0	0	0	1
C80 D1: ECOG score 0 (n=11,2,24,2,15,13)	14	10	1	17
C80 D1: ECOG score 1 (n=11,2,24,2,15,13)	1	1	1	5
C80 D1: ECOG score 2 (n=11,2,24,2,15,13)	0	0	0	2
C81 D1: ECOG score 0 (n=11,3,28,3,21,14)	19	10	2	21
C81 D1: ECOG score 1 (n=11,3,28,3,21,14)	2	1	1	6
C81 D1: ECOG score 2 (n=11,3,28,3,21,14)	0	0	0	1
C82 D1: ECOG score 0 (n=13,2,22,2,18,15)	16	11	1	16
C82 D1: ECOG score 1 (n=13,2,22,2,18,15)	2	2	1	5
C82 D1: ECOG score 2 (n=13,2,22,2,18,15)	0	0	0	1
C83 D1: ECOG score 0 (n=10,1,21,2,20,12)	17	8	0	16
C83 D1: ECOG score 1 (n=10,1,21,2,20,12)	3	2	1	5
C84 D1: ECOG score 0 (n=12,1,27,3,14,15)	13	11	1	21
C84 D1: ECOG score 1 (n=12,1,27,3,14,15)	1	1	0	5
C84 D1: ECOG score 2 (n=12,1,27,3,14,15)	0	0	0	1

C85 D1: ECOG score 0 (n=11,1,19,2,16,13)	14	11	0	14
C85 D1: ECOG score 1 (n=11,1,19,2,16,13)	2	0	0	5
C86 D1: ECOG score 0 (n=10,0,20,3,12,13)	11	9	99999	15
C86 D1: ECOG score 1 (n=10,0,20,3,12,13)	1	1	99999	4
C86 D1: ECOG score 2 (n=10,0,20,3,12,13)	0	0	99999	1
C87 D1: ECOG score 0 (n=10,2,28,2,16,12)	15	9	1	21
C87 D1: ECOG score 1 (n=10,2,28,2,16,12)	1	1	1	5
C87 D1: ECOG score 2 (n=10,2,28,2,16,12)	0	0	0	1
C87 D1: ECOG score 4 (n=10,2,28,2,16,12)	0	0	0	1
C88 D1: ECOG score 0 (n=8,0,18,3,13,11)	10	6	99999	14
C88 D1: ECOG score 1 (n=8,0,18,3,13,11)	3	2	99999	4
C88 D1: ECOG score 2 (n=8,0,18,3,13,11)	0	0	99999	0
C89 D1: ECOG score 0 (n=7,1,19,2,14,9)	13	6	0	15
C89 D1: ECOG score 1 (n=7,1,19,2,14,9)	1	1	1	4
C90 D1: ECOG score 0 (n=10,1,24,3,15,13)	14	8	1	18
C90 D1: ECOG score 1 (n=10,1,24,3,15,13)	1	2	0	5
C90 D1: ECOG score 2 (n=10,1,24,3,15,13)	0	0	0	1
C91 D1: ECOG score 0 (n=8,1,20,2,15,10)	12	7	0	15
C91 D1: ECOG score 1 (n=8,1,20,2,15,10)	3	1	1	5
C92 D1: ECOG score 0 (n=5,0,17,3,12,8)	10	5	99999	12
C92 D1: ECOG score 1 (n=5,0,17,3,12,8)	2	0	99999	5
C92 D1: ECOG score 2 (n=5,0,17,3,12,8)	0	0	99999	0
C93 D1: ECOG score 0 (n=7,2,24,2,16,9)	15	6	1	19
C93 D1: ECOG score 1 (n=7,2,24,2,16,9)	1	1	1	3
C93 D1: ECOG score 2 (n=7,2,24,2,16,9)	0	0	0	2
C94 D1: ECOG score 0 (n=8,0,18,2,14,10)	11	7	99999	14
C94 D1: ECOG score 1 (n=8,0,18,2,14,10)	3	1	99999	3
C94 D1: ECOG score 2 (n=8,0,18,2,14,10)	0	0	99999	1
C95 D1: ECOG score 0 (n=5,1,18,1,12,6)	11	4	0	13
C95 D1: ECOG score 1 (n=5,1,18,1,12,6)	1	1	1	3
C95 D1: ECOG score 2 (n=5,1,18,1,12,6)	0	0	0	2

C96 D1: ECOG score 0 (n=6,1,21,2,15,8)	14	6	0	16
C96 D1: ECOG score 1 (n=6,1,21,2,15,8)	1	0	1	4
C96 D1: ECOG score 2 (n=6,1,21,2,15,8)	0	0	0	1
C97 D1: ECOG score 0 (n=8,1,18,1,12,9)	9	8	0	16
C97 D1: ECOG score 1 (n=8,1,18,1,12,9)	3	0	1	1
C97 D1: ECOG score 2 (n=8,1,18,1,12,9)	0	0	0	1
C98 D1: ECOG score 0 (n=4,0,12,1,10,5)	7	4	99999	10
C98 D1: ECOG score 1 (n=4,0,12,1,10,5)	3	0	99999	1
C98 D1: ECOG score 2 (n=4,0,12,1,10,5)	0	0	99999	1
C99 D1: ECOG score 0 (n=6,2,17,2,14,8)	13	6	0	16
C99 D1: ECOG score 1 (n=6,2,17,2,14,8)	1	0	2	0
C99 D1: ECOG score 2 (n=6,2,17,2,14,8)	0	0	0	1
C100 D1: ECOG score 0 (n=6,0,12,1,12,7)	10	6	99999	11
C100 D1: ECOG score 1 (n=6,0,12,1,12,7)	2	0	99999	0
C100 D1: ECOG score 2 (n=6,0,12,1,12,7)	0	0	99999	1
C101 D1: ECOG score 0 (n=4,1,8,2,11,6)	9	4	0	8
C101 D1: ECOG score 1 (n=4,1,8,2,11,6)	2	0	1	0
C101 D1: ECOG score 2 (n=4,1,8,2,11,6)	0	0	0	0
C102 D1: ECOG score 0 (n=6,1,8,1,10,7)	8	6	0	8
C102 D1: ECOG score 1 (n=6,1,8,1,10,7)	1	0	1	0
C102 D1: ECOG score 2 (n=6,1,8,1,10,7)	1	0	0	0
C103 D1: ECOG score 0 (n=6,1,4,1,8,7)	6	6	0	4
C103 D1: ECOG score 1 (n=6,1,4,1,8,7)	2	0	1	0
C104 D1: ECOG score 0 (n=3,0,1,0,9,3)	9	2	99999	1
C104 D1: ECOG score 1 (n=3,0,1,0,9,3)	0	1	99999	0
C105 D1: ECOG score 0 (n=4,2,1,0,10,4)	10	4	0	1
C105 D1: ECOG score 1 (n=4,2,1,0,10,4)	0	0	2	0
C106 D1: ECOG score 0 (n=5,0,0,0,9,5)	6	5	99999	99999
C106 D1: ECOG score 1 (n=5,0,0,0,9,5)	3	0	99999	99999
C107 D1: ECOG score 0 (n=3,1,0,0,7,3)	6	3	0	99999
C107 D1: ECOG score 1 (n=3,1,0,0,7,3)	1	0	1	99999
C108 D1: ECOG score 0 (n=3,1,0,0,8,3)	8	3	0	99999
C108 D1: ECOG score 1 (n=3,1,0,0,8,3)	0	0	1	99999
C109 D1: ECOG score 0 (n=4,1,0,0,8,4)	7	4	0	99999
C109 D1: ECOG score 1 (n=4,1,0,0,8,4)	1	0	1	99999
C110 D1: ECOG score 0 (n=2,0,0,0,7,2)	7	2	99999	99999

C111 D1: ECOG score 0 (n=3,1,0,0,6,3)	6	3	0	99999
C111 D1: ECOG score 1 (n=3,1,0,0,6,3)	0	0	1	99999
C112 D1: ECOG score 0 (n=1,0,0,0,4,1)	4	1	99999	99999
C113 D1: ECOG score 0 (n=1,1,0,0,4,1)	3	1	0	99999
C113 D1: ECOG score 1 (n=1,1,0,0,4,1)	1	0	1	99999
C114 D1: ECOG score 0 (n=0,0,0,0,4,0)	3	99999	99999	99999
C114 D1: ECOG score 1 (n=0,0,0,0,4,0)	1	99999	99999	99999
C115 D1: ECOG score 0 (n=0,1,0,0,2,0)	1	99999	0	99999
C115 D1: ECOG score 1 (n=0,1,0,0,2,0)	1	99999	1	99999
C116 D1: ECOG score 0 (n=1,0,0,0,2,1)	2	1	99999	99999
C117 D1: ECOG score 0 (n=0,1,0,0,2,0)	2	99999	0	99999
C117 D1: ECOG score 1 (n=0,1,0,0,2,0)	0	99999	1	99999
C118 D1: ECOG score 0 (n=0,0,0,0,1,0)	1	99999	99999	99999
C119 D1: ECOG score 0 (n=0,0,0,0,1,1)	0	99999	99999	99999
30D safety fup ECOG score 0(n=76,60,75,30,64,106)	31	43	34	42
30D safety fup ECOG score 1(n=76,60,75,30,64,106)	26	27	21	27
30D safety fup ECOG score 2(n=76,60,75,30,64,106)	5	5	4	4
30D safety fup ECOG score 3(n=76,60,75,30,64,106)	1	0	1	2
30D safety fup ECOG score 4 (n=76,60,75,30,64,106)	1	1	0	0
C19 D1: ECOG score 4 (n=59,34,98,22,80,81)	0	0	0	1
C22 D1: ECOG score 2 (n=46,27,86,21,72,67)	0	0	0	1

End point values	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	84	276		
Units: subjects				
Baseline: ECOG score0 (n=192,186,257,84,192,276)	60	199		
Baseline: ECOG score1 (n=192,186,257,84,192,276)	24	77		
C2 D1: ECOG score 0 (n=182,181,256,80,188,262)	44	142		
C2 D1: ECOG score 1 (n=182,181,256,80,188,262)	32	111		
C2 D1: ECOG score 2 (n=182,181,256,80,188,262)	4	7		
C2 D1: ECOG score 3 (n=182,181,256,80,188,262)	0	2		
C2 D1: ECOG score 4 (n=182,181,256,80,188,262)	0	0		
C3 D1: ECOG score 0 (n=175,176,253,74,185,249)	40	130		
C3 D1: ECOG score 1 (n=175,176,253,74,185,249)	32	113		
C3 D1: ECOG score 2 (n=175,176,253,74,185,249)	2	6		

C4 D1: ECOG score 0 (n=164,158,250,68,179,232)	35	128		
C4 D1: ECOG score 1 (n=164,158,250,68,179,232)	30	96		
C4 D1: ECOG score 2 (n=164,158,250,68,179,232)	3	7		
C4 D1: ECOG score 3 (n=164,158,250,68,179,232)	0	1		
C5 D1: ECOG score 0 (n=158,143,239,66,174,224)	33	118		
C5 D1: ECOG score 1 (n=158,143,239,66,174,224)	31	100		
C5 D1: ECOG score 2 (n=158,143,239,66,174,224)	2	6		
C5 D1: ECOG score 3 (n=158,143,239,66,174,224)	0	0		
C5 D1: ECOG score 4 (n=158,143,239,66,174,224)	0	0		
C6 D1: ECOG score 0 (n=137,126,231,58,169,195)	29	97		
C6 D1: ECOG score 1 (n=137,126,231,58,169,195)	25	90		
C6 D1: ECOG score 2 (n=137,126,231,58,169,195)	3	6		
C6 D1: ECOG score 3 (n=137,126,231,58,169,195)	1	1		
C6 D1: ECOG score 4 (n=137,126,231,58,169,195)	0	1		
C7 D1: ECOG score 0 (n=129,111,218,55,159,184)	27	95		
C7 D1: ECOG score 1 (n=129,111,218,55,159,184)	27	87		
C7 D1: ECOG score 2 (n=129,111,218,55,159,184)	1	2		
C8 D1: ECOG score 0 (n=108,95,200,46,148,154)	22	77		
C8 D1: ECOG score 1 (n=108,95,200,46,148,154)	21	70		
C8 D1: ECOG score 2 (n=108,95,200,46,148,154)	3	6		
C8 D1: ECOG score 3 (n=108,95,200,46,148,154)	0	1		
C9 D1: ECOG score 0 (n=98,90,188,43,144,141)	22	72		
C9 D1: ECOG score 1 (n=98,90,188,43,144,141)	20	67		
C9 D1: ECOG score 2 (n=98,90,188,43,144,141)	0	1		
C9 D1: ECOG score 3 (n=98,90,188,43,144,141)	1	1		
C9 D1: ECOG score 4 (n=98,90,188,43,144,141)	0	0		
C10 D1: ECOG score 0 (n=88,73,171,37,129,125)	18	70		
C10 D1: ECOG score 1 (n=88,73,171,37,129,125)	18	53		
C10 D1: ECOG score 2 (n=88,73,171,37,129,125)	1	2		
C10 D1: ECOG score 3 (n=88,73,171,37,129,125)	0	0		
C11 D1: ECOG score 0 (n=85,62,158,36,121,121)	17	61		

C11 D1: ECOG score 1 (n=85,62,158,36,121,121)	16	56		
C11 D1: ECOG score 2 (n=85,62,158,36,121,121)	3	4		
C11 D1: ECOG score 3 (n=85,62,158,36,121,121)	0	0		
C12 D1: ECOG score 0 (n=77,50,152,30,110,107)	11	55		
C12 D1: ECOG score 1 (n=77,50,152,30,110,107)	18	49		
C12 D1: ECOG score 2 (n=77,50,152,30,110,107)	1	2		
C12 D1: ECOG score 3 (n=77,50,152,30,110,107)	0	1		
C12 D1: ECOG score 4 (n=77,50,152,30,110,107)	0	0		
C13 D1: ECOG score 0 (n=73,47,143,31,100,104)	14	55		
C13 D1: ECOG score 1 (n=73,47,143,31,100,104)	15	46		
C13 D1: ECOG score 2 (n=73,47,143,31,100,104)	2	3		
C13 D1: ECOG score 4 (n=73,47,143,31,100,104)	0	0		
C14 D1: ECOG score 0 (n=75,46,136,27,97,102)	15	62		
C14 D1: ECOG score 1 (n=75,46,136,27,97,102)	10	37		
C14 D1: ECOG score 2 (n=75,46,136,27,97,102)	2	2		
C14 D1: ECOG score 3 (n=75,46,136,27,97,102)	0	0		
C14 D1: ECOG score 4 (n=75,46,136,27,97,102)	0	1		
C15 D1: ECOG score 0 (n=72,41,126,25,94,97)	15	56		
C15 D1: ECOG score 1 (n=72,41,126,25,94,97)	8	38		
C15 D1: ECOG score 2 (n=72,41,126,25,94,97)	2	3		
C15 D1: ECOG score 3 (n=72,41,126,25,94,97)	0	0		
C15 D1: ECOG score 4 (n=72,41,126,25,94,97)	0	0		
C16 D1: ECOG score 0 (n=67,35,116,24,90,91)	13	54		
C16 D1: ECOG score 1 (n=67,35,116,24,90,91)	10	33		
C16 D1: ECOG score 2 (n=67,35,116,24,90,91)	1	4		
C16 D1: ECOG score 3 (n=67,35,116,24,90,91)	0	0		
C17 D1: ECOG score 0 (n=67,33,111,23,86,90)	12	51		
C17 D1: ECOG score 1 (n=67,33,111,23,86,90)	10	37		
C17 D1: ECOG score 2 (n=67,33,111,23,86,90)	1	2		
C18 D1: ECOG score 0 (n=60,33,104,23,85,83)	11	47		
C18 D1: ECOG score 1 (n=60,33,104,23,85,83)	11	35		

C18 D1: ECOG score 2 (n=60,33,104,23,85,83)	1	1		
C18 D1: ECOG score 3 (n=60,33,104,23,85,83)	0	0		
C19 D1: ECOG score 0 (n=59,34,98,22,80,81)	9	47		
C19 D1: ECOG score 1 (n=59,34,98,22,80,81)	12	32		
C19 D1: ECOG score 2 (n=59,34,98,22,80,81)	1	2		
C20 D1: ECOG score 0 (n=52,32,94,23,80,75)	11	42		
C20 D1: ECOG score 1 (n=52,32,94,23,80,75)	11	30		
C20 D1: ECOG score 2 (n=52,32,94,23,80,75)	1	3		
C20 D1: ECOG score 3 (n=52,32,94,23,80,75)	0	0		
C21 D1: ECOG score 0 (n=49,29,92,23,75,72)	10	39		
C21 D1: ECOG score 1 (n=49,29,92,23,75,72)	12	31		
C21 D1: ECOG score 2 (n=49,29,92,23,75,72)	1	2		
C22 D1: ECOG score 0 (n=46,27,86,21,72,67)	11	39		
C22 D1: ECOG score 1 (n=46,27,86,21,72,67)	8	24		
C22 D1: ECOG score 3 (n=46,27,86,21,72,67)	0	1		
C22 D1: ECOG score 4 (n=46,27,86,21,72,67)	0	2		
C23 D1: ECOG score 0 (n=40,26,81,19,67,59)	8	36		
C23 D1: ECOG score 1 (n=40,26,81,19,67,59)	9	21		
C23 D1: ECOG score 2 (n=40,26,81,19,67,59)	2	2		
C24 D1: ECOG score 0 (n=38,27,80,19,68,57)	9	37		
C24 D1: ECOG score 1 (n=38,27,80,19,68,57)	8	18		
C24 D1: ECOG score 2 (n=38,27,80,19,68,57)	2	2		
C25 D1: ECOG score 0 (n=38,25,80,19,64,57)	9	37		
C25 D1: ECOG score 1 (n=38,25,80,19,64,57)	8	18		
C25 D1: ECOG score 2 (n=38,25,80,19,64,57)	2	2		
C26 D1: ECOG score 0 (n=37,25,80,19,61,56)	9	36		
C26 D1: ECOG score 1 (n=37,25,80,19,61,56)	8	18		
C26 D1: ECOG score 2 (n=37,25,80,19,61,56)	2	2		
C27 D1: ECOG score 0 (n=36,23,76,19,58,55)	9	37		
C27 D1: ECOG score 1 (n=36,23,76,19,58,55)	8	16		
C27 D1: ECOG score 2 (n=36,23,76,19,58,55)	2	2		

C28 D1: ECOG score 0 (n=34,22,70,18,56,52)	7	32		
C28 D1: ECOG score 1 (n=34,22,70,18,56,52)	9	18		
C28 D1: ECOG score 2 (n=34,22,70,18,56,52)	2	2		
C29 D1: ECOG score 0 (n=34,21,67,16,56,50)	6	28		
C29 D1: ECOG score 1 (n=34,21,67,16,56,50)	8	20		
C29 D1: ECOG score 2 (n=34,21,67,16,56,50)	2	2		
C29 D1: ECOG score 3 (n=34,21,67,16,56,50)	0	0		
C30 D1: ECOG score 0 (n=32,21,69,15,55,47)	6	29		
C30 D1: ECOG score 1 (n=32,21,69,15,55,47)	7	16		
C30 D1: ECOG score 2 (n=32,21,69,15,55,47)	2	2		
C30 D1: ECOG score 4 (n=32,21,69,15,55,47)	0	0		
C31 D1: ECOG score 0 (n=32,21,62,15,55,47)	5	29		
C31 D1: ECOG score 1 (n=32,21,62,15,55,47)	8	16		
C31 D1: ECOG score 2 (n=32,21,62,15,55,47)	2	2		
C31 D1: ECOG score 4 (n=32,21,62,15,55,47)	0	0		
C32 D1: ECOG score 0 (n=30,20,63,14,52,44)	6	27		
C32 D1: ECOG score 1 (n=30,20,63,14,52,44)	6	14		
C32 D1: ECOG score 2 (n=30,20,63,14,52,44)	2	3		
C33 D1: ECOG score 0 (n=27,20,61,15,52,42)	7	28		
C33 D1: ECOG score 1 (n=27,20,61,15,52,42)	6	12		
C33 D1: ECOG score 2 (n=27,20,61,15,52,42)	2	2		
C34 D1: ECOG score 0 (n=26,19,61,15,52,41)	6	24		
C34 D1: ECOG score 1 (n=26,19,61,15,52,41)	7	15		
C34 D1: ECOG score 2 (n=26,19,61,15,52,41)	2	2		
C35 D1: ECOG score 0 (n=27,19,61,15,52,42)	7	26		
C35 D1: ECOG score 1 (n=27,19,61,15,52,42)	6	13		
C35 D1: ECOG score 2 (n=27,19,61,15,52,42)	2	2		
C36 D1: ECOG score 0 (n=25,18,60,15,51,40)	6	26		
C36 D1: ECOG score 1 (n=25,18,60,15,51,40)	7	12		
C36 D1: ECOG score 2 (n=25,18,60,15,51,40)	2	2		
C37 D1: ECOG score 0 (n=25,17,58,14,47,39)	5	23		

C37 D1: ECOG score 1 (n=25,17,58,14,47,39)	7	14		
C37 D1: ECOG score 2 (n=25,17,58,14,47,39)	2	2		
C38 D1: ECOG score 0 (n=25,17,59,13,48,38)	5	22		
C38 D1: ECOG score 1 (n=25,17,59,13,48,38)	6	14		
C38 D1: ECOG score 2 (n=25,17,59,13,48,38)	2	2		
C38 D1: ECOG score 3 (n=25,17,59,13,48,38)	0	0		
C39 D1: ECOG score 0 (n=25,16,57,14,47,39)	5	25		
C39 D1: ECOG score 1 (n=25,16,57,14,47,39)	7	12		
C39 D1: ECOG score 2 (n=25,16,57,14,47,39)	2	2		
C40 D1: ECOG score 0 (n=24,16,55,12,45,36)	3	20		
C40 D1: ECOG score 1 (n=24,16,55,12,45,36)	7	14		
C40 D1: ECOG score 2 (n=24,16,55,12,45,36)	2	2		
C41 D1: ECOG score 0 (n=23,15,56,13,44,36)	5	22		
C41 D1: ECOG score 1 (n=23,15,56,13,44,36)	6	12		
C41 D1: ECOG score 2 (n=23,15,56,13,44,36)	2	2		
C42 D1: ECOG score 0 (n=23,14,55,13,41,36)	4	22		
C42 D1: ECOG score 1 (n=23,14,55,13,41,36)	7	12		
C42 D1: ECOG score 2 (n=23,14,55,13,41,36)	2	2		
C43 D1: ECOG score 0 (n=23,14,54,13,39,36)	4	22		
C43 D1: ECOG score 1 (n=23,14,54,13,39,36)	7	12		
C43 D1: ECOG score 2 (n=23,14,54,13,39,36)	2	2		
C44 D1: ECOG score 0 (n=23,14,54,13,41,36)	5	22		
C44 D1: ECOG score 1 (n=23,14,54,13,41,36)	6	12		
C44 D1: ECOG score 2 (n=23,14,54,13,41,36)	2	2		
C45 D1: ECOG score 0 (n=23,14,52,10,40,33)	4	21		
C45 D1: ECOG score 1 (n=23,14,52,10,40,33)	6	12		
C46 D1: ECOG score 0 (n=21,11,49,10,40,31)	4	21		
C46 D1: ECOG score 1 (n=21,11,49,10,40,31)	6	10		
C47 D1: ECOG score 0 (n=23,10,49,10,40,33)	4	22		
C47 D1: ECOG score 1 (n=23,10,49,10,40,33)	6	11		
C48 D1: ECOG score 0 (n=22,11,50,9,38,31)	3	20		

C48 D1: ECOG score 1 (n=22,11,50,9,38,31)	6	11		
C48 D1: ECOG score 3 (n=22,11,50,9,38,31)	0	0		
C49 D1: ECOG score 0 (n=21,10,47,9,38,30)	3	17		
C49 D1: ECOG score 1 (n=21,10,47,9,38,30)	6	13		
C49 D1: ECOG score 2 (n=21,10,47,9,38,30)	0	0		
C49 D1: ECOG score 3 (n=21,10,47,9,38,30)	0	0		
C50 D1: ECOG score 0 (n=21,10,46,8,39,29)	3	19		
C50 D1: ECOG score 1 (n=21,10,46,8,39,29)	5	10		
C50 D1: ECOG score 2 (n=21,10,46,8,39,29)	0	0		
C51 D1: ECOG score 0 (n=19,10,43,8,38,27)	2	18		
C51 D1: ECOG score 1 (n=19,10,43,8,38,27)	5	8		
C51 D1: ECOG score 2 (n=19,10,43,8,38,27)	1	1		
C52 D1: ECOG score 0 (n=20,10,44,8,38,28)	1	15		
C52 D1: ECOG score 1 (n=20,10,44,8,38,28)	7	3		
C52 D1: ECOG score 2 (n=20,10,44,8,38,28)	0	0		
C53 D1: ECOG score 0 (n=20,10,42,7,37,27)	2	16		
C53 D1: ECOG score 1 (n=20,10,42,7,37,27)	5	11		
C53 D1: ECOG score 2 (n=20,10,42,7,37,27)	0	0		
C54 D1: ECOG score 0 (n=20,10,42,8,33,28)	2	16		
C54 D1: ECOG score 1 (n=20,10,42,8,33,28)	6	12		
C54 D1: ECOG score 2 (n=20,10,42,8,33,28)	0	0		
C55 D1: ECOG score 0 (n=20,10,41,7,36,27)	4	19		
C55 D1: ECOG score 1 (n=20,10,41,7,36,27)	3	8		
C55 D1: ECOG score 2 (n=20,10,41,7,36,27)	0	0		
C56 D1: ECOG score 0 (n=20,9,40,7,36,27)	3	16		
C56 D1: ECOG score 1 (n=20,9,40,7,36,27)	4	11		
C56 D1: ECOG score 2 (n=20,9,40,7,36,27)	0	0		
C57 D1: ECOG score 0 (n=19,8,39,7,35,26)	3	18		
C57 D1: ECOG score 1 (n=19,8,39,7,35,26)	4	8		
C57 D1: ECOG score 2 (n=19,8,39,7,35,26)	0	0		
C58 D1: ECOG score 0 (n=19,10,37,7,34,26)	4	18		

C58 D1: ECOG score 1 (n=19,10,37,7,34,26)	3	8		
C58 D1: ECOG score 2 (n=19,10,37,7,34,26)	0	0		
C59 D1: ECOG score 0 (n=18,8,36,6,33,24)	3	16		
C59 D1: ECOG score 1 (n=18,8,36,6,33,24)	3	8		
C59 D1: ECOG score 2 (n=18,8,36,6,33,24)	0	0		
C60 D1: ECOG score 0 (n=17,8,38,5,32,22)	3	16		
C60 D1: ECOG score 1 (n=17,8,38,5,32,22)	2	6		
C60 D1: ECOG score 2 (n=17,8,38,5,32,22)	0	0		
C61 D1: ECOG score 0 (n=18,8,35,5,30,23)	3	16		
C61 D1: ECOG score 1 (n=18,8,35,5,30,23)	2	7		
C61 D1: ECOG score 2 (n=18,8,35,5,30,23)	0	0		
C61 D1: ECOG score 3 (n=18,8,35,5,30,23)	0	0		
C62 D1: ECOG score 0 (n=17,7,35,5,29,22)	3	16		
C62 D1: ECOG score 1 (n=17,7,35,5,29,22)	2	6		
C62 D1: ECOG score 2 (n=17,7,35,5,29,22)	0	0		
C63 D1: ECOG score 0 (n=17,7,33,5,28,22)	3	16		
C63 D1: ECOG score 1 (n=17,7,33,5,28,22)	2	6		
C63 D1: ECOG score 2 (n=17,7,33,5,28,22)	0	0		
C64 D1: ECOG score 0 (n=17,7,32,5,28,22)	2	13		
C64 D1: ECOG score 1 (n=17,7,32,5,28,22)	3	9		
C64 D1: ECOG score 2 (n=17,7,32,5,28,22)	0	0		
C65 D1: ECOG score 0 (n=16,7,29,4,28,20)	2	15		
C65 D1: ECOG score 1 (n=16,7,29,4,28,20)	2	5		
C65 D1: ECOG score 2 (n=16,7,29,4,28,20)	0	0		
C66 D1: ECOG score 0 (n=17,7,32,4,28,21)	2	14		
C66 D1: ECOG score 1 (n=17,7,32,4,28,21)	2	7		
C66 D1: ECOG score 2 (n=17,7,32,4,28,21)	0	0		
C67 D1: ECOG score 0 (n=15,7,29,5,28,20)	3	16		
C67 D1: ECOG score 1 (n=15,7,29,5,28,20)	2	4		
C67 D1: ECOG score 2 (n=15,7,29,5,28,20)	0	0		
C68 D1: ECOG score 0 (n=15,6,29,5,28,20)	2	15		

C68 D1: ECOG score 1 (n=15,6,29,5,28,20)	3	5		
C68 D1: ECOG score 2 (n=15,6,29,5,28,20)	0	0		
C69 D1: ECOG score 0 (n=14,6,30,5,26,19)	1	13		
C69 D1: ECOG score 1 (n=14,6,30,5,26,19)	3	5		
C69 D1: ECOG score 2 (n=14,6,30,5,26,19)	1	1		
C70 D1: ECOG score 0 (n=14,6,29,5,27,19)	2	13		
C70 D1: ECOG score 1 (n=14,6,29,5,27,19)	3	6		
C70 D1: ECOG score 2 (n=14,6,29,5,27,19)	0	0		
C71 D1: ECOG score 0 (n=14,6,24,4,26,18)	1	13		
C71 D1: ECOG score 1 (n=14,6,24,4,26,18)	3	5		
C71 D1: ECOG score 2 (n=14,6,24,4,26,18)	0	0		
C72 D1: ECOG score 0 (n=14,5,32,4,28,18)	2	13		
C72 D1: ECOG score 1 (n=14,5,32,4,28,18)	2	5		
C72 D1: ECOG score 2 (n=14,5,32,4,28,18)	0	0		
C73 D1: ECOG score 0 (n=13,5,24,4,25,17)	1	13		
C73 D1: ECOG score 1 (n=13,5,24,4,25,17)	3	4		
C73 D1: ECOG score 2 (n=13,5,24,4,25,17)	0	0		
C74 D1: ECOG score 0 (n=14,5,25,5,26,19)	2	15		
C74 D1: ECOG score 1 (n=14,5,25,5,26,19)	3	4		
C74 D1: ECOG score 2 (n=14,5,25,5,26,19)	0	0		
C75 D1: ECOG score 0 (n=13,5,29,3,25,16)	1	13		
C75 D1: ECOG score 1 (n=13,5,29,3,25,16)	2	3		
C75 D1: ECOG score 2 (n=13,5,29,3,25,16)	0	0		
C76 D1: ECOG score 0 (n=14,3,24,4,24,18)	1	14		
C76 D1: ECOG score 1 (n=14,3,24,4,24,18)	3	4		
C76 D1: ECOG score 2 (n=14,3,24,4,24,18)	0	0		
C77 D1: ECOG score 0 (n=12,3,21,4,20,16)	0	11		
C77 D1: ECOG score 1 (n=12,3,21,4,20,16)	4	5		
C78 D1: ECOG score 0 (n=13,3,31,2,19,15)	0	12		
C78 D1: ECOG score 1 (n=13,3,31,2,19,15)	2	3		
C78 D1: ECOG score 2 (n=13,3,31,2,19,15)	0	0		

C79 D1: ECOG score 0 (n=14,2,22,2,21,16)	0	12		
C79 D1: ECOG score 1 (n=14,2,22,2,21,16)	2	4		
C79 D1: ECOG score 2 (n=14,2,22,2,21,16)	0	0		
C80 D1: ECOG score 0 (n=11,2,24,2,15,13)	0	10		
C80 D1: ECOG score 1 (n=11,2,24,2,15,13)	2	3		
C80 D1: ECOG score 2 (n=11,2,24,2,15,13)	0	0		
C81 D1: ECOG score 0 (n=11,3,28,3,21,14)	0	10		
C81 D1: ECOG score 1 (n=11,3,28,3,21,14)	3	4		
C81 D1: ECOG score 2 (n=11,3,28,3,21,14)	0	0		
C82 D1: ECOG score 0 (n=13,2,22,2,18,15)	0	11		
C82 D1: ECOG score 1 (n=13,2,22,2,18,15)	2	4		
C82 D1: ECOG score 2 (n=13,2,22,2,18,15)	0	0		
C83 D1: ECOG score 0 (n=10,1,21,2,20,12)	0	8		
C83 D1: ECOG score 1 (n=10,1,21,2,20,12)	2	4		
C84 D1: ECOG score 0 (n=12,1,27,3,14,15)	0	11		
C84 D1: ECOG score 1 (n=12,1,27,3,14,15)	3	4		
C84 D1: ECOG score 2 (n=12,1,27,3,14,15)	0	0		
C85 D1: ECOG score 0 (n=11,1,19,2,16,13)	0	11		
C85 D1: ECOG score 1 (n=11,1,19,2,16,13)	2	2		
C86 D1: ECOG score 0 (n=10,0,20,3,12,13)	0	9		
C86 D1: ECOG score 1 (n=10,0,20,3,12,13)	3	4		
C86 D1: ECOG score 2 (n=10,0,20,3,12,13)	0	0		
C87 D1: ECOG score 0 (n=10,2,28,2,16,12)	0	9		
C87 D1: ECOG score 1 (n=10,2,28,2,16,12)	2	3		
C87 D1: ECOG score 2 (n=10,2,28,2,16,12)	0	0		
C87 D1: ECOG score 4 (n=10,2,28,2,16,12)	0	0		
C88 D1: ECOG score 0 (n=8,0,18,3,13,11)	0	6		
C88 D1: ECOG score 1 (n=8,0,18,3,13,11)	2	4		
C88 D1: ECOG score 2 (n=8,0,18,3,13,11)	1	1		
C89 D1: ECOG score 0 (n=7,1,19,2,14,9)	0	6		
C89 D1: ECOG score 1 (n=7,1,19,2,14,9)	2	3		

C90 D1: ECOG score 0 (n=10,1,24,3,15,13)	0	8		
C90 D1: ECOG score 1 (n=10,1,24,3,15,13)	2	4		
C90 D1: ECOG score 2 (n=10,1,24,3,15,13)	1	1		
C91 D1: ECOG score 0 (n=8,1,20,2,15,10)	0	7		
C91 D1: ECOG score 1 (n=8,1,20,2,15,10)	2	3		
C92 D1: ECOG score 0 (n=5,0,17,3,12,8)	0	5		
C92 D1: ECOG score 1 (n=5,0,17,3,12,8)	2	2		
C92 D1: ECOG score 2 (n=5,0,17,3,12,8)	1	1		
C93 D1: ECOG score 0 (n=7,2,24,2,16,9)	0	6		
C93 D1: ECOG score 1 (n=7,2,24,2,16,9)	2	3		
C93 D1: ECOG score 2 (n=7,2,24,2,16,9)	0	0		
C94 D1: ECOG score 0 (n=8,0,18,2,14,10)	0	7		
C94 D1: ECOG score 1 (n=8,0,18,2,14,10)	1	2		
C94 D1: ECOG score 2 (n=8,0,18,2,14,10)	1	1		
C95 D1: ECOG score 0 (n=5,1,18,1,12,6)	0	4		
C95 D1: ECOG score 1 (n=5,1,18,1,12,6)	1	2		
C95 D1: ECOG score 2 (n=5,1,18,1,12,6)	0	0		
C96 D1: ECOG score 0 (n=6,1,21,2,15,8)	0	6		
C96 D1: ECOG score 1 (n=6,1,21,2,15,8)	1	1		
C96 D1: ECOG score 2 (n=6,1,21,2,15,8)	1	1		
C97 D1: ECOG score 0 (n=8,1,18,1,12,9)	0	8		
C97 D1: ECOG score 1 (n=8,1,18,1,12,9)	1	1		
C97 D1: ECOG score 2 (n=8,1,18,1,12,9)	0	0		
C98 D1: ECOG score 0 (n=4,0,12,1,10,5)	0	4		
C98 D1: ECOG score 1 (n=4,0,12,1,10,5)	1	1		
C98 D1: ECOG score 2 (n=4,0,12,1,10,5)	0	0		
C99 D1: ECOG score 0 (n=6,2,17,2,14,8)	0	6		
C99 D1: ECOG score 1 (n=6,2,17,2,14,8)	1	1		
C99 D1: ECOG score 2 (n=6,2,17,2,14,8)	1	1		
C100 D1: ECOG score 0 (n=6,0,12,1,12,7)	0	6		
C100 D1: ECOG score 1 (n=6,0,12,1,12,7)	1	1		

C100 D1: ECOG score 2 (n=6,0,12,1,12,7)	0	0		
C101 D1: ECOG score 0 (n=4,1,8,2,11,6)	0	4		
C101 D1: ECOG score 1 (n=4,1,8,2,11,6)	1	1		
C101 D1: ECOG score 2 (n=4,1,8,2,11,6)	1	1		
C102 D1: ECOG score 0 (n=6,1,8,1,10,7)	0	6		
C102 D1: ECOG score 1 (n=6,1,8,1,10,7)	1	1		
C102 D1: ECOG score 2 (n=6,1,8,1,10,7)	0	0		
C103 D1: ECOG score 0 (n=6,1,4,1,8,7)	0	6		
C103 D1: ECOG score 1 (n=6,1,4,1,8,7)	1	1		
C104 D1: ECOG score 0 (n=3,0,1,0,9,3)	99999	2		
C104 D1: ECOG score 1 (n=3,0,1,0,9,3)	99999	1		
C105 D1: ECOG score 0 (n=4,2,1,0,10,4)	99999	4		
C105 D1: ECOG score 1 (n=4,2,1,0,10,4)	99999	0		
C106 D1: ECOG score 0 (n=5,0,0,0,9,5)	99999	5		
C106 D1: ECOG score 1 (n=5,0,0,0,9,5)	99999	0		
C107 D1: ECOG score 0 (n=3,1,0,0,7,3)	99999	3		
C107 D1: ECOG score 1 (n=3,1,0,0,7,3)	99999	0		
C108 D1: ECOG score 0 (n=3,1,0,0,8,3)	99999	3		
C108 D1: ECOG score 1 (n=3,1,0,0,8,3)	99999	0		
C109 D1: ECOG score 0 (n=4,1,0,0,8,4)	99999	4		
C109 D1: ECOG score 1 (n=4,1,0,0,8,4)	99999	0		
C110 D1: ECOG score 0 (n=2,0,0,0,7,2)	99999	2		
C111 D1: ECOG score 0 (n=3,1,0,0,6,3)	99999	3		
C111 D1: ECOG score 1 (n=3,1,0,0,6,3)	99999	0		
C112 D1: ECOG score 0 (n=1,0,0,0,4,1)	99999	1		
C113 D1: ECOG score 0 (n=1,1,0,0,4,1)	99999	1		
C113 D1: ECOG score 1 (n=1,1,0,0,4,1)	99999	0		
C114 D1: ECOG score 0 (n=0,0,0,0,4,0)	99999	99999		
C114 D1: ECOG score 1 (n=0,0,0,0,4,0)	99999	99999		
C115 D1: ECOG score 0 (n=0,1,0,0,2,0)	99999	99999		
C115 D1: ECOG score 1 (n=0,1,0,0,2,0)	99999	99999		
C116 D1: ECOG score 0 (n=1,0,0,0,2,1)	99999	1		
C117 D1: ECOG score 0 (n=0,1,0,0,2,0)	99999	99999		
C117 D1: ECOG score 1 (n=0,1,0,0,2,0)	99999	99999		
C118 D1: ECOG score 0 (n=0,0,0,0,1,0)	99999	99999		
C119 D1: ECOG score 0 (n=0,0,0,0,1,1)	99999	99999		
30D safety fup ECOG score 0(n=76,60,75,30,64,106)	13	56		
30D safety fup ECOG score 1(n=76,60,75,30,64,106)	11	38		
30D safety fup ECOG score 2(n=76,60,75,30,64,106)	5	10		
30D safety fup ECOG score 3(n=76,60,75,30,64,106)	1	1		
30D safety fup ECOG score 4 (n=76,60,75,30,64,106)	0	1		
C19 D1: ECOG score 4 (n=59,34,98,22,80,81)	0	0		

C22 D1: ECOG score 2 (n=46,27,86,21,72,67)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Plasma Concentrations of LGX 818

End point title	Part 1: Plasma Concentrations of LGX 818[22]

End point description:

Pharmacokinetic analysis set included all subjects who received at least one dose of LGX818 or MEK162 and had at least one evaluable post-baseline LGX818 or MEK162 concentration measurement. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1: pre-dose, 0.5, 1.5, anytime between 4 to 8 hours post dose; Cycle 2 Day 1: pre-dose; Cycle 3 Day 1: pre-dose

Notes:

[22] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	172		
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
C1 D1: pre-dose (n=172,175)	18.6 (± 125)	58.1 (± 513)		
C1 D1: 0.5 hours post dose (n=145,159)	1640 (± 2400)	1190 (± 1790)		
C1 D1: 1.5 hours post dose (n=116,122)	6860 (± 3680)	4090 (± 2100)		
C1 D1: 4 to 8 hours post dose (n=142,147)	3400 (± 2010)	1850 (± 925)		
C2 D1: pre-dose (73,119)	119 (± 468)	73.6 (± 405)		
C3 D1: pre-dose (n=74,98)	150 (± 697)	53.8 (± 256)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Plasma Concentrations of LGX 818

End point title	Part 2: Plasma Concentrations of LGX 818[23]

End point description:

Pharmacokinetic analysis set included all subjects who received at least one dose of LGX818 or MEK162 and had at least one evaluable post-baseline LGX818 or MEK162 concentration measurement. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1: pre-dose, 0.5, 1.5, anytime between 4 to 8 hours post dose; Cycle 2 Day 1: pre-dose; Cycle 3 Day 1: pre-dose

Notes:

[23] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 2: LGX818 300 mg	Part 1 + Part 2: LGX818 300 mg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	242	80	252	
Units: ng/ml				
arithmetic mean (standard deviation)				
C1 D1: pre-dose (n=242,80,252)	5.02 (± 77.8)	0.0145 (± 0.130)	39.7 (± 424)	
C1 D1: 0.5 hours post dose (n=207,68,213)	1360 (± 2000)	1370 (± 2170)	1250 (± 1910)	
C1 D1: 1.5 hours post dose (n=220,73,189)	4390 (± 2380)	4310 (± 2570)	4170 (± 2290)	
C1 D1: 4 to 8 hours post dose (n=185,66,208)	2420 (± 1270)	2250 (± 1170)	1980 (± 1020)	
C2 D1: pre-dose (175,32,105)	121 (± 483)	29.5 (± 99.9)	60.1 (± 342)	
C3 D1: pre-dose (n=151,27,101)	74.1 (± 322)	79.5 (± 291)	60.6 (± 265)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Plasma Concentrations of MEK162

End point title	Part 1: Plasma Concentrations of MEK162[24]

End point description:

Pharmacokinetic analysis set included all subjects who received at least one dose of LGX818 or MEK162 and had at least one evaluable post-baseline LGX818 or MEK162 concentration measurement. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1: pre-dose, 0.5, 1.5, anytime between 4 to 8 hours post dose; Cycle 2 Day 1: pre-dose; Cycle 3 Day 1: pre-dose

Notes:

[24] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: ng/ml				
arithmetic mean (standard deviation)				
C1 D1: pre-dose (n=167)	2.95 (± 30.7)			
C1 D1: 0.5 hours post dose (n=151)	426 (± 410)			
C1 D1: 1.5 hours post dose (n=117)	832 (± 527)			
C1 D1: 4 to 8 hours post dose (n=138)	330 (± 226)			
C2 D1: pre-dose (n=77)	81.0 (± 106)			
C3 D1: pre-dose (n=65)	68.1 (± 101)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Plasma Concentrations of MEK162

End point title	Part 2: Plasma Concentrations of MEK162[25]

End point description:

Pharmacokinetic analysis set included all subjects who received at least one dose of LGX818 or MEK162 and had at least one evaluable post-baseline LGX818 or MEK162 concentration measurement. Here, Number of subjects analyzed signifies the number of subjects evaluable for this endpoint and n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1: pre-dose, 0.5, 1.5, anytime between 4 to 8 hours post dose; Cycle 2 Day 1: pre-dose; Cycle 3 Day 1: pre-dose

Notes:

[25] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: ng/ml				
arithmetic mean (standard deviation)				
C1 D1: pre-dose (n=215)	1.68 (± 24.3)			
C1 D1: 0.5 hours post dose (n=191)	366 (± 347)			
C1 D1: 1.5 hours post dose (n=196)	642 (± 337)			
C1 D1: 4 to 8 hours post dose (n=169)	287 (± 175)			
C2 D1: pre-dose (n=98)	72.3 (± 62.6)			
C3 D1: pre-dose (n=94)	73.2 (± 89.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Time to Definitive 1 Point Deterioration in Eastern Cooperative Oncology Group Performance Status (ECOG PS)

End point title	Part 1 and Part 2: Time to Definitive 1 Point Deterioration in Eastern Cooperative Oncology Group Performance Status (ECOG PS)[26]

End point description:

ECOG: subjects performance status was measured on a 6-point scale: 0= fully active/able to carry on all pre-disease activities without restriction; 1=restricted in physically strenuous activity but ambulatory & able to carry out work of a light & sedentary nature; 2=ambulatory &= capable of all self-care, but unable to carry out any work activities, up & about more than 50 percent (%) of waking hours; 3= capable of only limited self-care, confined to bed/chair >50% of waking hours; 4=completely disabled, cannot carry on any self-care, totally confined to bed/chair: 5= dead. Definitive deterioration was defined as death due to any cause/decrease in ECOG PS by at least one category from baseline score with no subsequent improvement. Safety analysis set. Number of subjects analyzed =number of subjects evaluable for this endpoint. 99999=data could not be estimated due to low number of subjects with events. Planned to report combined result data of Part 1 and Part 2 for LGX818 300 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to 30 days from last dose of study drug (up to maximum of 417.7, 471.4 and 415.4 weeks of treatment for Combo 300, LGX818 300 and Part 1 and 2 arms, respectively)

Notes:

[26] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 1 + Part 2: LGX818 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	192	186	257	270
Units: months				
median (confidence interval 95%)	99999 (53.4 to 99999)	20.9 (11.1 to 99999)	83.4 (52.4 to 99999)	24.8 (14.8 to 50.1)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: PFS by BIRC in Combo 450 Group as Compared to Vemurafenib Group: Final OS and Follow-up Efficacy and Safety Data as of End of Study

End point title	Part 1: PFS by BIRC in Combo 450 Group as Compared to

	Vemurafenib Group: Final OS and Follow-up Efficacy and Safety Data as of End of Study[27]

End point description:

PFS was defined as the time from the date of randomization to the date of the first documented PD or death due to any cause, whichever occured first. PFS was determined based on tumor assessment (RECIST version 1.1 criteria) as per BIRC/central review and survival information. If a subject did not have an event at the time of the analysis cut-off or at the start of any new anti-cancer therapy, data was censored at the date of last adequate tumor assessment. PD was defined as at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must demonstrate an absolute increase of at least 5 square millimeter (mm^2). Full analysis set (FAS) included all randomized subjects.

End point type	Other pre-specified

End point timeframe:

From randomization until documented PD, initiation of new anti-cancer therapy, censoring date or death, whichever occurred first (up to maximum of 471.7 and 465.4 weeks of treatment for Combo 3450 and vemurafenib, respectively)

Notes:

[27] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: Vemurafenib 960 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	191		
Units: months				
median (confidence interval 95%)	14.9 (11.0 to 20.2)	7.3 (5.6 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Part 1: PFS by BIRC in Combo 450 Group as Compared to LGX818 Group: Final OS and Follow-up Efficacy and Safety Data as of End of Study

End point title	Part 1: PFS by BIRC in Combo 450 Group as Compared to LGX818 Group: Final OS and Follow-up Efficacy and Safety Data as of End of Study[28]

End point description:

PFS was defined as the time from the date of randomization to the date of the first documented PD or death due to any cause, whichever occurred first. PFS was determined based on tumor assessment (RECIST version 1.1 criteria) as per BIRC and survival information. If a subject did not have an event at the time of the analysis cut-off or at the start of any new anti-cancer therapy, data was censored at the date of last adequate tumor assessment. PD was defined as at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must demonstrate an absolute increase of at least 5 mm^2. FAS included all randomized subjects.

End point type	Other pre-specified

End point timeframe:

From randomization until documented PD, initiation of new anti-cancer therapy, censoring date or death, whichever occurred first (up to maximum of 471.7 and 465.4 weeks of treatment for Combo 3450 and vemurafenib, respectively)

Notes:

[28] - 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: This endpoint was summarized for specified reporting arms only.

End point values	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 1: LGX818 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	194		
Units: months				
median (confidence interval 95%)	14.9 (11.0 to 20.2)	9.6 (7.4 to 14.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1: Baseline up to 30 days from last dose of study drug (up to maximum of 417.7, 465.4, 471.4, 471.4 and 415.4 weeks of treatment for LGX818 300, vemurafenib, combo 300, combo 450 and Part 1 and 2 arms, respectively)

Adverse event reporting additional description:

Same event may appear as AE and serious AE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety analysis population evaluated.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Part 1: Vemurafenib 960 mg BID

Reporting group description:

Subjects received 960 mg of LGX818 according to the locally approved prescribing information twice daily for each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)

Reporting group description:

Subjects received 300 mg of LGX818 orally once daily along with 45 mg of MEK162 twice daily for each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 1: LGX818 300 mg

Reporting group description:

Subjects received 300 mg of LGX818 orally once daily for each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)

Reporting group description:

Subjects received 450 milligram (mg) of LGX818 orally once daily (QD) along with 45 mg of MEK162 twice daily (BID) for each 28 day treatment cycle until progressive disease (PD) as confirmed by Blinded Independent Review Committee (BIRC), withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Reporting group title	Part 2: LGX818 300 mg

Reporting group description:

Subjects received 300 mg of LGX818 orally once daily for each 28 day treatment cycle until PD as confirmed by BIRC, withdrawal of consent, intolerable toxicity, study discontinuation, lost to follow-up or death.

Serious adverse events	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 1: LGX818 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 186 (41.94%)	98 / 257 (38.13%)	71 / 192 (36.98%)
number of deaths (all causes)	145	171	125
number of deaths resulting from adverse events	6	14	8

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial Tumour Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Metastases To Bone			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases To Central Nervous System			
subjects affected / exposed	3 / 186 (1.61%)	4 / 257 (1.56%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Metastases To Meninges			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Rectal Adenocarcinoma			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Malignant Melanoma In Situ			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer Pain			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatofibrosarcoma Protuberans			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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

Malignant Melanoma			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal Cell Carcinoma			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	1 / 1	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional Cell Carcinoma			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Superficial Spreading Melanoma Stage Unspecified			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous Cell Carcinoma			
subjects affected / exposed	3 / 186 (1.61%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Metastatic Malignant Melanoma			
subjects affected / exposed	2 / 186 (1.08%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastasis			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases To Adrenals			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases To Spine			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Metastases To Bladder			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Tumour Associated Fever			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Tumour Pain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Plasma Cell Myeloma			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Benign neoplasm			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Benign bone neoplasm			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Myeloproliferative neoplasm			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Endometrial cancer			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Colon cancer			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Lung adenocarcinoma			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Breast cancer			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Vascular disorders			
Superficial vein thrombosis			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Deep Vein Thrombosis			
subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	0 / 192 (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
Embolism			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Circulatory Collapse			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Thrombosis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Giant cell arteritis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Death			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General Physical Health Deterioration			
subjects affected / exposed	6 / 186 (3.23%)	4 / 257 (1.56%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	2 / 6	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
Pyrexia			
subjects affected / exposed	2 / 186 (1.08%)	2 / 257 (0.78%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	1 / 2	0 / 2	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Inflammation			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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			

subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	4 / 192 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema Peripheral			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Performance Status Decreased			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Immune system disorders			
Contrast Media Allergy			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Hypersensitivity			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Hypersensitivity			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast Pain			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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

Ovarian cyst			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	3 / 186 (1.61%)	2 / 257 (0.78%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 3	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Pulmonary Alveolar Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
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 Arrest			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Dyspnoea			
subjects affected / exposed	3 / 186 (1.61%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Mediastinal Shift			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Epistaxis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Lung Infiltration			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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 Failure			
subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Pneumonitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Nasal polyps			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Psychiatric disorders			
Confusional State			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental Status Changes			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Depression Suicidal			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Completed Suicide			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Depression			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Post-Traumatic Stress Disorder			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Agitation			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Product issues			
Device Failure			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Intraocular Pressure Increased			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-Reactive Protein Increased			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Lipase Increased			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White Blood Cell Count Increased			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	0 / 192 (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
Myocardial Necrosis Marker Increased			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph Node Palpable			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Troponin Increased			

subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Injury, poisoning and procedural complications			
Radiation Necrosis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Multiple Injuries			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Acetabulum Fracture			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Spinal Compression Fracture			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Compression Fracture			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Spinal Fracture			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Seroma			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Face injury			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Chest injury			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Toxicity to various agents			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Skin abrasion			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Jaw fracture			

subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Rib fracture			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Procedural pain			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated incisional hernia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Intestinal anastomosis complication			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 186 (0.00%)	3 / 257 (1.17%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Coronary Syndrome			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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

Bundle Branch Block Left			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Acute Myocardial Infarction			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial Fibrillation			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial Effusion			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Palpitations			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Myocardial Ischaemia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left Ventricular Failure			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Tachycardia			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	0 / 192 (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
Pericarditis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Cardio-Respiratory Arrest			
subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
Cardiac Tamponade			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Tachyarrhythmia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Congestive cardiomyopathy			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Cardiac hypertrophy			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Nervous system disorders			
Cerebral Haemorrhage			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Balance Disorder			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Somnolence			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Hemiparesis			
subjects affected / exposed	3 / 186 (1.61%)	2 / 257 (0.78%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 186 (0.54%)	2 / 257 (0.78%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 186 (0.54%)	4 / 257 (1.56%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Coma			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Cervicobrachial Syndrome			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Transient Ischaemic Attack			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Dizziness			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Spinal Cord Compression			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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 Paralysis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain Stem Syndrome			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Brain Oedema			

subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 186 (0.00%)	3 / 257 (1.17%)	0 / 192 (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
Paraesthesia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glial Scar			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intercostal Neuralgia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Intracranial Pressure Increased			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Nervous System Disorder			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Facial Paresis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	1 / 186 (0.54%)	5 / 257 (1.95%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restless Legs Syndrome			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Cerebellar Ischaemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Aphasia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Facial Nerve Disorder			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Paresis Cranial Nerve			

subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Vertebral Artery Dissection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Tremor			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Ischaemic Stroke			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Speech Disorder			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Hypertensive Encephalopathy			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Guillain-Barre Syndrome			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Monoplegia			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Cerebrovascular Accident			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Diplegia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Motor Dysfunction			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bell's palsy			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Hemihypoaesthesia			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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			
Anaemia			
subjects affected / exposed	2 / 186 (1.08%)	6 / 257 (2.33%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 2	3 / 6	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Lymphopenia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Febrile neutropenia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node pain			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Eye disorders			
Normal Tension Glaucoma			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Detachment			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central serous chorioretinopathy			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Retinal Artery Occlusion			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Uveitis			
subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Vein Occlusion			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Angle closure glaucoma			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Cataract			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Visual impairment			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Vision blurred			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Vogt-Koyanagi-Hara da disease			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	6 / 192 (3.13%)
occurrences causally related to treatment / all	1 / 2	0 / 0	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Diverticulum			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Diarrhoea			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	6 / 192 (3.13%)
occurrences causally related to treatment / all	0 / 0	1 / 2	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Abdominal Pain Upper			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 186 (0.54%)	2 / 257 (0.78%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Anal Incontinence			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Anal Fistula			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Distension			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			

subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Pancreatitis Acute			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Pancreatitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Inguinal Hernia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Diarrhoea Haemorrhagic			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
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 Intestine Perforation			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			
subjects affected / exposed	2 / 186 (1.08%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	2 / 257 (0.78%)	0 / 192 (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
Constipation			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Oesophagitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Gastritis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Enterocolitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Pancreatic fistula			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
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 stenosis			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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			
Jaundice			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Cholecystitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Hepatic failure			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Cholecystitis acute			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Rash Erythematous			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granuloma Annulare			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Erythema Nodosum			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Drug Eruption			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Dermatitis Bullous			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Dermatitis Allergic			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Cutaneous Vasculitis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Rash			
subjects affected / exposed	3 / 186 (1.61%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 186 (0.54%)	5 / 257 (1.95%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	1 / 1	2 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Urethral			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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 Failure			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Renal Impairment			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary Incontinence			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Ureteric Obstruction			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	0 / 192 (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
Urinary Tract Disorder			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Ureterolithiasis			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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 Retention			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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 vasculitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Glomerulonephritis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Musculoskeletal and connective tissue disorders			
Pain In Extremity			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Intervertebral Disc Disorder			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Fracture Pain			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Groin Pain			

subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility Decreased			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal Pain			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 0	2 / 2	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Pain			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back Pain			
subjects affected / exposed	3 / 186 (1.61%)	1 / 257 (0.39%)	4 / 192 (2.08%)
occurrences causally related to treatment / all	0 / 3	0 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	3 / 186 (1.61%)	1 / 257 (0.39%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	3 / 3	2 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Rheumatoid Arthritis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Polymyalgia Rheumatica			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Muscular Weakness			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Spinal stenosis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Osteoarthritis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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			
Cellulitis Streptococcal			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Chorioretinitis			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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			
subjects affected / exposed	3 / 186 (1.61%)	4 / 257 (1.56%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cellulitis			
subjects affected / exposed	1 / 186 (0.54%)	2 / 257 (0.78%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 186 (0.00%)	4 / 257 (1.56%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Campylobacter Gastroenteritis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Sepsis			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Infected Seroma			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Escherichia Sepsis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Diverticulitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Encephalitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Peritonsillar Abscess			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal Sepsis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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			
subjects affected / exposed	1 / 186 (0.54%)	3 / 257 (1.17%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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 Difficile Colitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Appendicitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Myelitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Peritoneal Abscess			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Nasopharyngitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Liver Abscess			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Influenza			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Zika virus infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Wound infection			

subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Peritonitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Osteomyelitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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
Kidney infection			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	0 / 192 (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			
Hyperkalaemia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 186 (0.54%)	2 / 257 (0.78%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	1 / 4	3 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Decreased Appetite			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hyperlipidaemia			

subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Hyperglycaemia			
subjects affected / exposed	0 / 186 (0.00%)	0 / 257 (0.00%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 186 (0.54%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	0 / 192 (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
Hyponatraemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (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

Serious adverse events	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 2: LGX818 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	85 / 192 (44.27%)	31 / 84 (36.90%)	
number of deaths (all causes)	136	60	
number of deaths resulting from adverse events	10	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial Tumour Haemorrhage			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases To Bone			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases To Central Nervous System			
subjects affected / exposed	3 / 192 (1.56%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Metastases To Meninges			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal Adenocarcinoma			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma In Situ			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer Pain			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatofibrosarcoma Protuberans			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Cell Carcinoma			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Haemorrhage			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional Cell Carcinoma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial Spreading Melanoma Stage Unspecified			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic Malignant Melanoma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastasis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases To Adrenals			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases To Spine			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases To Bladder			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Associated Fever			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Pain			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma Cell Myeloma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign bone neoplasm			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative neoplasm			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Superficial vein thrombosis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep Vein Thrombosis			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory Collapse			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Giant cell arteritis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Cardiac Chest Pain			

subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
General Physical Health Deterioration			
subjects affected / exposed	3 / 192 (1.56%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	7 / 192 (3.65%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pain			
subjects affected / exposed	1 / 192 (0.52%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema Peripheral			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance Status Decreased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Contrast Media Allergy			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Hypersensitivity			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Breast Pain			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	3 / 192 (1.56%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Alveolar Haemorrhage			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Arrest			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinal Shift			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epistaxis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Infiltration			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional State			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Status Changes			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression Suicidal			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed Suicide			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Depression			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-Traumatic Stress Disorder			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device Failure			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular Pressure Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Enzyme Increased			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-Reactive Protein Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White Blood Cell Count Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Necrosis Marker Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph Node Palpable			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Radiation Necrosis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Injuries			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acetabulum Fracture			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression Fracture			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Fracture			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin abrasion			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated incisional hernia			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal anastomosis complication			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Coronary Syndrome			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle Branch Block Left			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrioventricular Block First Degree			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Myocardial Infarction			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial Effusion			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Ischaemia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left Ventricular Failure			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure			

subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-Respiratory Arrest			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Tamponade			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac hypertrophy			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral Haemorrhage			
subjects affected / exposed	3 / 192 (1.56%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Balance Disorder			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 192 (0.52%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dysarthria			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cervicobrachial Syndrome			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Ischaemic Attack			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Cord Compression			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Paralysis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Stem Syndrome			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Oedema			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glial Scar			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal Neuralgia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial Pressure Increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous System Disorder			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Paresis			
subjects affected / exposed	0 / 192 (0.00%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restless Legs Syndrome			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed Level Of Consciousness			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar Ischaemia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Nerve Disorder			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paresis Cranial Nerve			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral Artery Dissection			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Speech Disorder			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Encephalopathy			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre Syndrome			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoplegia			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			

subjects affected / exposed	1 / 192 (0.52%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplegia			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor Dysfunction			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bell's palsy			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 192 (0.52%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemihypoaesthesia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	5 / 192 (2.60%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	2 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node pain			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Normal Tension Glaucoma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal Detachment			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central serous chorioretinopathy			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal Artery Occlusion			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal Vein Occlusion			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angle closure glaucoma			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vogt-Koyanagi-Hara da disease			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	5 / 192 (2.60%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	2 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 192 (1.56%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer Haemorrhage			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diverticulum			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Incontinence			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Fistula			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Distension			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Haemorrhage			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia			
subjects affected / exposed	2 / 192 (1.04%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea Haemorrhagic			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Gastrointestinal Haemorrhage			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic fistula			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash Erythematous			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granuloma Annulare			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema Nodosum			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Eruption			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Bullous			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Allergic			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous Vasculitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			

subjects affected / exposed	4 / 192 (2.08%)	3 / 84 (3.57%)	
occurrences causally related to treatment / all	1 / 4	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus Urethral			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Impairment			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Incontinence			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric Obstruction			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Disorder			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Retention			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal vasculitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain In Extremity			
subjects affected / exposed	1 / 192 (0.52%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Disorder			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture Pain			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin Pain			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mobility Decreased			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal Pain			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Pain			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 192 (0.00%)	3 / 84 (3.57%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid Arthritis			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia Rheumatica			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular Weakness			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis Streptococcal			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chorioretinitis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	3 / 192 (1.56%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis			
subjects affected / exposed	2 / 192 (1.04%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	3 / 192 (1.56%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter Gastroenteritis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Sepsis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Seroma			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Sepsis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar Abscess			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal Sepsis			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Infection			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal Abscess			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			

subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Infection			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Abscess			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Zika virus infection			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased Appetite			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperlipidaemia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 192 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: Vemurafenib 960 mg BID	Part 2: LGX818 300 mg QD+MEK162 45 mg BID (Combo 300)	Part 1: LGX818 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	185 / 186 (99.46%)	152 / 257 (59.14%)	190 / 192 (98.96%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	32 / 186 (17.20%)	18 / 257 (7.00%)	21 / 192 (10.94%)
occurrences (all)	46	22	27
Seborrhoeic keratosis			
subjects affected / exposed	13 / 186 (6.99%)	6 / 257 (2.33%)	13 / 192 (6.77%)
occurrences (all)	16	8	14
Keratoacanthoma			
subjects affected / exposed	22 / 186 (11.83%)	5 / 257 (1.95%)	15 / 192 (7.81%)
occurrences (all)	25	6	17
Melanocytic naevus			

subjects affected / exposed	7 / 186 (3.76%)	6 / 257 (2.33%)	18 / 192 (9.38%)
occurrences (all)	10	6	31
Squamous cell carcinoma			
subjects affected / exposed	10 / 186 (5.38%)	0 / 257 (0.00%)	3 / 192 (1.56%)
occurrences (all)	18	0	3
Vascular disorders			
Hypertension			
subjects affected / exposed	24 / 186 (12.90%)	38 / 257 (14.79%)	12 / 192 (6.25%)
occurrences (all)	44	71	19
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	56 / 186 (30.11%)	67 / 257 (26.07%)	51 / 192 (26.56%)
occurrences (all)	90	92	77
Asthenia			
subjects affected / exposed	35 / 186 (18.82%)	45 / 257 (17.51%)	42 / 192 (21.88%)
occurrences (all)	72	81	74
Pyrexia			
subjects affected / exposed	54 / 186 (29.03%)	50 / 257 (19.46%)	32 / 192 (16.67%)
occurrences (all)	68	87	48
Oedema peripheral			
subjects affected / exposed	20 / 186 (10.75%)	36 / 257 (14.01%)	18 / 192 (9.38%)
occurrences (all)	28	42	22
Influenza like illness			
subjects affected / exposed	3 / 186 (1.61%)	14 / 257 (5.45%)	15 / 192 (7.81%)
occurrences (all)	5	17	17
Xerosis			
subjects affected / exposed	8 / 186 (4.30%)	2 / 257 (0.78%)	17 / 192 (8.85%)
occurrences (all)	11	2	23
Chills			
subjects affected / exposed	10 / 186 (5.38%)	16 / 257 (6.23%)	13 / 192 (6.77%)
occurrences (all)	13	19	14
Pain			
subjects affected / exposed	0 / 186 (0.00%)	9 / 257 (3.50%)	0 / 192 (0.00%)
occurrences (all)	0	10	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	15 / 186 (8.06%)	21 / 257 (8.17%)	24 / 192 (12.50%)
occurrences (all)	17	27	34
Dyspnoea			
subjects affected / exposed	14 / 186 (7.53%)	12 / 257 (4.67%)	10 / 192 (5.21%)
occurrences (all)	18	16	10
Oropharyngeal pain			
subjects affected / exposed	12 / 186 (6.45%)	6 / 257 (2.33%)	10 / 192 (5.21%)
occurrences (all)	16	8	10
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 186 (2.15%)	11 / 257 (4.28%)	8 / 192 (4.17%)
occurrences (all)	4	12	8
Insomnia			
subjects affected / exposed	15 / 186 (8.06%)	20 / 257 (7.78%)	37 / 192 (19.27%)
occurrences (all)	17	21	50
Depression			
subjects affected / exposed	3 / 186 (1.61%)	5 / 257 (1.95%)	10 / 192 (5.21%)
occurrences (all)	3	5	11
Investigations			
Blood creatinine increased			
subjects affected / exposed	12 / 186 (6.45%)	14 / 257 (5.45%)	4 / 192 (2.08%)
occurrences (all)	18	23	4
Blood creatine phosphokinase increased			
subjects affected / exposed	4 / 186 (2.15%)	67 / 257 (26.07%)	4 / 192 (2.08%)
occurrences (all)	5	228	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	20 / 186 (10.75%)	44 / 257 (17.12%)	22 / 192 (11.46%)
occurrences (all)	27	100	41
Alanine aminotransferase increased			
subjects affected / exposed	15 / 186 (8.06%)	36 / 257 (14.01%)	11 / 192 (5.73%)
occurrences (all)	20	66	16
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 186 (8.06%)	27 / 257 (10.51%)	9 / 192 (4.69%)
occurrences (all)	17	52	10

Blood alkaline phosphatase increased			
subjects affected / exposed	10 / 186 (5.38%)	16 / 257 (6.23%)	6 / 192 (3.13%)
occurrences (all)	12	25	7
Ejection fraction decreased			
subjects affected / exposed	1 / 186 (0.54%)	0 / 257 (0.00%)	4 / 192 (2.08%)
occurrences (all)	1	0	4
Weight decreased			
subjects affected / exposed	20 / 186 (10.75%)	10 / 257 (3.89%)	30 / 192 (15.63%)
occurrences (all)	31	13	39
Blood bilirubin increased			
subjects affected / exposed	14 / 186 (7.53%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences (all)	29	0	0
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	20 / 186 (10.75%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences (all)	40	0	1
Fall			
subjects affected / exposed	1 / 186 (0.54%)	13 / 257 (5.06%)	4 / 192 (2.08%)
occurrences (all)	1	18	4
Nervous system disorders			
Headache			
subjects affected / exposed	38 / 186 (20.43%)	50 / 257 (19.46%)	56 / 192 (29.17%)
occurrences (all)	56	79	77
Dizziness			
subjects affected / exposed	8 / 186 (4.30%)	28 / 257 (10.89%)	11 / 192 (5.73%)
occurrences (all)	11	40	17
Dysgeusia			
subjects affected / exposed	16 / 186 (8.60%)	10 / 257 (3.89%)	22 / 192 (11.46%)
occurrences (all)	20	12	25
Paraesthesia			
subjects affected / exposed	12 / 186 (6.45%)	9 / 257 (3.50%)	18 / 192 (9.38%)
occurrences (all)	16	9	20
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 186 (10.22%)	35 / 257 (13.62%)	15 / 192 (7.81%)
occurrences (all)	46	61	53

Neutropenia			
subjects affected / exposed	3 / 186 (1.61%)	14 / 257 (5.45%)	3 / 192 (1.56%)
occurrences (all)	3	23	3
Eye disorders			
Cataract			
subjects affected / exposed	8 / 186 (4.30%)	16 / 257 (6.23%)	7 / 192 (3.65%)
occurrences (all)	9	17	9
Retinal detachment			
subjects affected / exposed	0 / 186 (0.00%)	15 / 257 (5.84%)	2 / 192 (1.04%)
occurrences (all)	0	25	6
Vision blurred			
subjects affected / exposed	4 / 186 (2.15%)	29 / 257 (11.28%)	4 / 192 (2.08%)
occurrences (all)	5	36	4
Macular oedema			
subjects affected / exposed	2 / 186 (1.08%)	0 / 257 (0.00%)	0 / 192 (0.00%)
occurrences (all)	2	0	0
Dry eye			
subjects affected / exposed	13 / 186 (6.99%)	12 / 257 (4.67%)	14 / 192 (7.29%)
occurrences (all)	14	12	17
Blepharitis			
subjects affected / exposed	11 / 186 (5.91%)	10 / 257 (3.89%)	10 / 192 (5.21%)
occurrences (all)	12	13	13
Lacrimation increased			
subjects affected / exposed	0 / 186 (0.00%)	1 / 257 (0.39%)	0 / 192 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	4 / 186 (2.15%)	0 / 257 (0.00%)	8 / 192 (4.17%)
occurrences (all)	4	0	11
Visual field defect			
subjects affected / exposed	3 / 186 (1.61%)	13 / 257 (5.06%)	5 / 192 (2.60%)
occurrences (all)	3	13	8
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	29 / 186 (15.59%)	53 / 257 (20.62%)	51 / 192 (26.56%)
occurrences (all)	40	90	71
Constipation			

subjects affected / exposed	13 / 186 (6.99%)	53 / 257 (20.62%)	32 / 192 (16.67%)
occurrences (all)	14	64	43
Abdominal pain			
subjects affected / exposed	13 / 186 (6.99%)	32 / 257 (12.45%)	14 / 192 (7.29%)
occurrences (all)	19	45	20
Abdominal pain upper			
subjects affected / exposed	20 / 186 (10.75%)	40 / 257 (15.56%)	18 / 192 (9.38%)
occurrences (all)	25	50	20
Dyspepsia			
subjects affected / exposed	8 / 186 (4.30%)	0 / 257 (0.00%)	9 / 192 (4.69%)
occurrences (all)	8	0	12
Stomatitis			
subjects affected / exposed	11 / 186 (5.91%)	9 / 257 (3.50%)	17 / 192 (8.85%)
occurrences (all)	12	9	25
Dysphagia			
subjects affected / exposed	10 / 186 (5.38%)	0 / 257 (0.00%)	7 / 192 (3.65%)
occurrences (all)	11	0	7
Diarrhoea			
subjects affected / exposed	64 / 186 (34.41%)	92 / 257 (35.80%)	29 / 192 (15.10%)
occurrences (all)	135	184	33
Nausea			
subjects affected / exposed	65 / 186 (34.95%)	73 / 257 (28.40%)	69 / 192 (35.94%)
occurrences (all)	78	113	96
Skin and subcutaneous tissue disorders			
Keratosis pilaris			
subjects affected / exposed	43 / 186 (23.12%)	8 / 257 (3.11%)	33 / 192 (17.19%)
occurrences (all)	52	8	40
Dry skin			
subjects affected / exposed	43 / 186 (23.12%)	26 / 257 (10.12%)	58 / 192 (30.21%)
occurrences (all)	49	30	83
Hyperkeratosis			
subjects affected / exposed	54 / 186 (29.03%)	29 / 257 (11.28%)	76 / 192 (39.58%)
occurrences (all)	91	34	148
Rash			
subjects affected / exposed	67 / 186 (36.02%)	30 / 257 (11.67%)	49 / 192 (25.52%)
occurrences (all)	107	43	70

Alopecia			
subjects affected / exposed	70 / 186 (37.63%)	36 / 257 (14.01%)	108 / 192 (56.25%)
occurrences (all)	76	38	142
Pruritus			
subjects affected / exposed	41 / 186 (22.04%)	28 / 257 (10.89%)	59 / 192 (30.73%)
occurrences (all)	47	43	80
Palmoplantar keratoderma			
subjects affected / exposed	33 / 186 (17.74%)	20 / 257 (7.78%)	51 / 192 (26.56%)
occurrences (all)	49	26	98
Erythema			
subjects affected / exposed	33 / 186 (17.74%)	19 / 257 (7.39%)	32 / 192 (16.67%)
occurrences (all)	59	25	38
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	26 / 186 (13.98%)	13 / 257 (5.06%)	99 / 192 (51.56%)
occurrences (all)	34	19	300
Skin hyperpigmentation			
subjects affected / exposed	3 / 186 (1.61%)	3 / 257 (1.17%)	16 / 192 (8.33%)
occurrences (all)	3	3	19
Rash maculo-papular			
subjects affected / exposed	27 / 186 (14.52%)	12 / 257 (4.67%)	18 / 192 (9.38%)
occurrences (all)	50	19	22
Actinic keratosis			
subjects affected / exposed	10 / 186 (5.38%)	0 / 257 (0.00%)	6 / 192 (3.13%)
occurrences (all)	14	0	7
Photosensitivity reaction			
subjects affected / exposed	47 / 186 (25.27%)	0 / 257 (0.00%)	7 / 192 (3.65%)
occurrences (all)	71	0	7
Rash papular			
subjects affected / exposed	7 / 186 (3.76%)	4 / 257 (1.56%)	12 / 192 (6.25%)
occurrences (all)	7	6	12
Vitiligo			
subjects affected / exposed	0 / 186 (0.00%)	11 / 257 (4.28%)	0 / 192 (0.00%)
occurrences (all)	0	13	0
Solar dermatitis			

subjects affected / exposed	17 / 186 (9.14%)	0 / 257 (0.00%)	1 / 192 (0.52%)
occurrences (all)	23	0	1
Skin lesion			
subjects affected / exposed	14 / 186 (7.53%)	0 / 257 (0.00%)	8 / 192 (4.17%)
occurrences (all)	16	0	8
Skin exfoliation			
subjects affected / exposed	4 / 186 (2.15%)	1 / 257 (0.39%)	11 / 192 (5.73%)
occurrences (all)	4	1	12
Papule			
subjects affected / exposed	0 / 186 (0.00%)	4 / 257 (1.56%)	0 / 192 (0.00%)
occurrences (all)	0	5	0
Hair texture abnormal			
subjects affected / exposed	7 / 186 (3.76%)	7 / 257 (2.72%)	10 / 192 (5.21%)
occurrences (all)	7	7	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	86 / 186 (46.24%)	74 / 257 (28.79%)	96 / 192 (50.00%)
occurrences (all)	162	121	227
Myalgia			
subjects affected / exposed	34 / 186 (18.28%)	38 / 257 (14.79%)	55 / 192 (28.65%)
occurrences (all)	47	47	105
Pain in extremity			
subjects affected / exposed	27 / 186 (14.52%)	38 / 257 (14.79%)	44 / 192 (22.92%)
occurrences (all)	42	53	78
Back pain			
subjects affected / exposed	10 / 186 (5.38%)	51 / 257 (19.84%)	33 / 192 (17.19%)
occurrences (all)	11	67	40
Muscle spasms			
subjects affected / exposed	4 / 186 (2.15%)	25 / 257 (9.73%)	7 / 192 (3.65%)
occurrences (all)	8	37	11
Musculoskeletal pain			
subjects affected / exposed	4 / 186 (2.15%)	5 / 257 (1.95%)	12 / 192 (6.25%)
occurrences (all)	5	7	19
Muscular weakness			

subjects affected / exposed	4 / 186 (2.15%)	5 / 257 (1.95%)	7 / 192 (3.65%)
occurrences (all)	5	5	9
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	20 / 186 (10.75%)	35 / 257 (13.62%)	15 / 192 (7.81%)
occurrences (all)	33	63	33
Upper respiratory tract infection			
subjects affected / exposed	7 / 186 (3.76%)	19 / 257 (7.39%)	8 / 192 (4.17%)
occurrences (all)	7	34	19
Influenza			
subjects affected / exposed	10 / 186 (5.38%)	0 / 257 (0.00%)	9 / 192 (4.69%)
occurrences (all)	12	0	10
Folliculitis			
subjects affected / exposed	10 / 186 (5.38%)	0 / 257 (0.00%)	8 / 192 (4.17%)
occurrences (all)	11	0	11
Conjunctivitis			
subjects affected / exposed	15 / 186 (8.06%)	9 / 257 (3.50%)	9 / 192 (4.69%)
occurrences (all)	19	9	11
Oral candidiasis			
subjects affected / exposed	0 / 186 (0.00%)	6 / 257 (2.33%)	0 / 192 (0.00%)
occurrences (all)	0	8	0
Urinary tract infection			
subjects affected / exposed	5 / 186 (2.69%)	21 / 257 (8.17%)	8 / 192 (4.17%)
occurrences (all)	5	32	11
Gastroenteritis			
subjects affected / exposed	3 / 186 (1.61%)	0 / 257 (0.00%)	2 / 192 (1.04%)
occurrences (all)	4	0	2
Bronchitis			
subjects affected / exposed	6 / 186 (3.23%)	0 / 257 (0.00%)	7 / 192 (3.65%)
occurrences (all)	6	0	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	36 / 186 (19.35%)	30 / 257 (11.67%)	41 / 192 (21.35%)
occurrences (all)	43	42	50
Hyperglycaemia			

subjects affected / exposed	2 / 186 (1.08%)	14 / 257 (5.45%)	6 / 192 (3.13%)
occurrences (all)	8	34	9

Non-serious adverse events	Part 1: LGX818 450 mg QD+MEK162 45 mg BID (Combo 450)	Part 2: LGX818 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	189 / 192 (98.44%)	82 / 84 (97.62%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	16 / 192 (8.33%)	13 / 84 (15.48%)	
occurrences (all)	18	13	
Seborrhoeic keratosis			
subjects affected / exposed	12 / 192 (6.25%)	5 / 84 (5.95%)	
occurrences (all)	18	6	
Keratoacanthoma			
subjects affected / exposed	8 / 192 (4.17%)	10 / 84 (11.90%)	
occurrences (all)	11	14	
Melanocytic naevus			
subjects affected / exposed	6 / 192 (3.13%)	6 / 84 (7.14%)	
occurrences (all)	7	6	
Squamous cell carcinoma			
subjects affected / exposed	3 / 192 (1.56%)	0 / 84 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	36 / 192 (18.75%)	5 / 84 (5.95%)	
occurrences (all)	53	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	57 / 192 (29.69%)	26 / 84 (30.95%)	
occurrences (all)	100	37	
Asthenia			
subjects affected / exposed	44 / 192 (22.92%)	16 / 84 (19.05%)	
occurrences (all)	103	22	
Pyrexia			

subjects affected / exposed	36 / 192 (18.75%)	13 / 84 (15.48%)	
occurrences (all)	63	31	
Oedema peripheral			
subjects affected / exposed	25 / 192 (13.02%)	5 / 84 (5.95%)	
occurrences (all)	40	8	
Influenza like illness			
subjects affected / exposed	12 / 192 (6.25%)	2 / 84 (2.38%)	
occurrences (all)	20	2	
Xerosis			
subjects affected / exposed	5 / 192 (2.60%)	1 / 84 (1.19%)	
occurrences (all)	7	1	
Chills			
subjects affected / exposed	9 / 192 (4.69%)	3 / 84 (3.57%)	
occurrences (all)	9	5	
Pain			
subjects affected / exposed	0 / 192 (0.00%)	7 / 84 (8.33%)	
occurrences (all)	0	8	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 192 (12.50%)	5 / 84 (5.95%)	
occurrences (all)	32	8	
Dyspnoea			
subjects affected / exposed	20 / 192 (10.42%)	7 / 84 (8.33%)	
occurrences (all)	28	7	
Oropharyngeal pain			
subjects affected / exposed	7 / 192 (3.65%)	5 / 84 (5.95%)	
occurrences (all)	8	5	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	18 / 192 (9.38%)	7 / 84 (8.33%)	
occurrences (all)	21	8	
Insomnia			
subjects affected / exposed	23 / 192 (11.98%)	14 / 84 (16.67%)	
occurrences (all)	35	18	
Depression			

subjects affected / exposed	6 / 192 (3.13%)	1 / 84 (1.19%)	
occurrences (all)	7	1	
Investigations			
Blood creatinine increased			
subjects affected / exposed	14 / 192 (7.29%)	1 / 84 (1.19%)	
occurrences (all)	28	2	
Blood creatine phosphokinase increased			
subjects affected / exposed	52 / 192 (27.08%)	0 / 84 (0.00%)	
occurrences (all)	142	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	30 / 192 (15.63%)	7 / 84 (8.33%)	
occurrences (all)	68	11	
Alanine aminotransferase increased			
subjects affected / exposed	23 / 192 (11.98%)	1 / 84 (1.19%)	
occurrences (all)	41	1	
Aspartate aminotransferase increased			
subjects affected / exposed	19 / 192 (9.90%)	1 / 84 (1.19%)	
occurrences (all)	27	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	16 / 192 (8.33%)	2 / 84 (2.38%)	
occurrences (all)	17	3	
Ejection fraction decreased			
subjects affected / exposed	12 / 192 (6.25%)	0 / 84 (0.00%)	
occurrences (all)	22	0	
Weight decreased			
subjects affected / exposed	7 / 192 (3.65%)	8 / 84 (9.52%)	
occurrences (all)	12	9	
Blood bilirubin increased			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences (all)	2	0	

Fall			
subjects affected / exposed	11 / 192 (5.73%)	2 / 84 (2.38%)	
occurrences (all)	14	2	
Nervous system disorders			
Headache			
subjects affected / exposed	52 / 192 (27.08%)	24 / 84 (28.57%)	
occurrences (all)	79	38	
Dizziness			
subjects affected / exposed	32 / 192 (16.67%)	5 / 84 (5.95%)	
occurrences (all)	46	7	
Dysgeusia			
subjects affected / exposed	11 / 192 (5.73%)	6 / 84 (7.14%)	
occurrences (all)	15	6	
Paraesthesia			
subjects affected / exposed	19 / 192 (9.90%)	8 / 84 (9.52%)	
occurrences (all)	28	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	39 / 192 (20.31%)	6 / 84 (7.14%)	
occurrences (all)	100	13	
Neutropenia			
subjects affected / exposed	10 / 192 (5.21%)	0 / 84 (0.00%)	
occurrences (all)	20	0	
Eye disorders			
Cataract			
subjects affected / exposed	17 / 192 (8.85%)	2 / 84 (2.38%)	
occurrences (all)	21	2	
Retinal detachment			
subjects affected / exposed	14 / 192 (7.29%)	0 / 84 (0.00%)	
occurrences (all)	41	0	
Vision blurred			
subjects affected / exposed	30 / 192 (15.63%)	2 / 84 (2.38%)	
occurrences (all)	39	2	
Macular oedema			
subjects affected / exposed	13 / 192 (6.77%)	0 / 84 (0.00%)	
occurrences (all)	22	0	
Dry eye			

subjects affected / exposed	16 / 192 (8.33%)	1 / 84 (1.19%)	
occurrences (all)	20	1	
Blepharitis			
subjects affected / exposed	11 / 192 (5.73%)	4 / 84 (4.76%)	
occurrences (all)	13	4	
Lacrimation increased			
subjects affected / exposed	0 / 192 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	5	
Visual impairment			
subjects affected / exposed	10 / 192 (5.21%)	0 / 84 (0.00%)	
occurrences (all)	13	0	
Visual field defect			
subjects affected / exposed	18 / 192 (9.38%)	1 / 84 (1.19%)	
occurrences (all)	27	1	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	65 / 192 (33.85%)	19 / 84 (22.62%)	
occurrences (all)	134	27	
Constipation			
subjects affected / exposed	50 / 192 (26.04%)	11 / 84 (13.10%)	
occurrences (all)	70	13	
Abdominal pain			
subjects affected / exposed	35 / 192 (18.23%)	5 / 84 (5.95%)	
occurrences (all)	57	7	
Abdominal pain upper			
subjects affected / exposed	25 / 192 (13.02%)	5 / 84 (5.95%)	
occurrences (all)	39	7	
Dyspepsia			
subjects affected / exposed	17 / 192 (8.85%)	0 / 84 (0.00%)	
occurrences (all)	21	0	
Stomatitis			
subjects affected / exposed	8 / 192 (4.17%)	4 / 84 (4.76%)	
occurrences (all)	11	5	
Dysphagia			
subjects affected / exposed	4 / 192 (2.08%)	0 / 84 (0.00%)	
occurrences (all)	4	0	

Diarrhoea			
subjects affected / exposed	75 / 192 (39.06%)	8 / 84 (9.52%)	
occurrences (all)	213	14	
Nausea			
subjects affected / exposed	84 / 192 (43.75%)	27 / 84 (32.14%)	
occurrences (all)	184	34	
Skin and subcutaneous tissue disorders			
Keratosis pilaris			
subjects affected / exposed	9 / 192 (4.69%)	10 / 84 (11.90%)	
occurrences (all)	13	10	
Dry skin			
subjects affected / exposed	34 / 192 (17.71%)	19 / 84 (22.62%)	
occurrences (all)	42	20	
Hyperkeratosis			
subjects affected / exposed	29 / 192 (15.10%)	36 / 84 (42.86%)	
occurrences (all)	46	76	
Rash			
subjects affected / exposed	36 / 192 (18.75%)	27 / 84 (32.14%)	
occurrences (all)	46	38	
Alopecia			
subjects affected / exposed	29 / 192 (15.10%)	29 / 84 (34.52%)	
occurrences (all)	33	41	
Pruritus			
subjects affected / exposed	28 / 192 (14.58%)	19 / 84 (22.62%)	
occurrences (all)	45	22	
Palmoplantar keratoderma			
subjects affected / exposed	19 / 192 (9.90%)	17 / 84 (20.24%)	
occurrences (all)	30	27	
Erythema			
subjects affected / exposed	17 / 192 (8.85%)	13 / 84 (15.48%)	
occurrences (all)	22	17	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	16 / 192 (8.33%)	32 / 84 (38.10%)	
occurrences (all)	22	95	
Skin hyperpigmentation			

subjects affected / exposed	4 / 192 (2.08%)	4 / 84 (4.76%)	
occurrences (all)	4	4	
Rash maculo-papular			
subjects affected / exposed	6 / 192 (3.13%)	3 / 84 (3.57%)	
occurrences (all)	7	5	
Actinic keratosis			
subjects affected / exposed	10 / 192 (5.21%)	0 / 84 (0.00%)	
occurrences (all)	11	0	
Photosensitivity reaction			
subjects affected / exposed	7 / 192 (3.65%)	0 / 84 (0.00%)	
occurrences (all)	9	0	
Rash papular			
subjects affected / exposed	5 / 192 (2.60%)	2 / 84 (2.38%)	
occurrences (all)	8	3	
Vitiligo			
subjects affected / exposed	0 / 192 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	6	
Solar dermatitis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	5 / 192 (2.60%)	0 / 84 (0.00%)	
occurrences (all)	5	0	
Skin exfoliation			
subjects affected / exposed	2 / 192 (1.04%)	0 / 84 (0.00%)	
occurrences (all)	2	0	
Papule			
subjects affected / exposed	0 / 192 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	5	
Hair texture abnormal			
subjects affected / exposed	7 / 192 (3.65%)	2 / 84 (2.38%)	
occurrences (all)	7	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	64 / 192 (33.33%)	39 / 84 (46.43%)	
occurrences (all)	123	68	
Myalgia			
subjects affected / exposed	32 / 192 (16.67%)	22 / 84 (26.19%)	
occurrences (all)	47	38	
Pain in extremity			
subjects affected / exposed	24 / 192 (12.50%)	14 / 84 (16.67%)	
occurrences (all)	39	38	
Back pain			
subjects affected / exposed	30 / 192 (15.63%)	8 / 84 (9.52%)	
occurrences (all)	44	11	
Muscle spasms			
subjects affected / exposed	26 / 192 (13.54%)	1 / 84 (1.19%)	
occurrences (all)	35	1	
Musculoskeletal pain			
subjects affected / exposed	11 / 192 (5.73%)	6 / 84 (7.14%)	
occurrences (all)	14	10	
Muscular weakness			
subjects affected / exposed	11 / 192 (5.73%)	5 / 84 (5.95%)	
occurrences (all)	13	8	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	28 / 192 (14.58%)	7 / 84 (8.33%)	
occurrences (all)	56	11	
Upper respiratory tract infection			
subjects affected / exposed	19 / 192 (9.90%)	3 / 84 (3.57%)	
occurrences (all)	28	3	
Influenza			
subjects affected / exposed	12 / 192 (6.25%)	0 / 84 (0.00%)	
occurrences (all)	15	0	
Folliculitis			
subjects affected / exposed	7 / 192 (3.65%)	0 / 84 (0.00%)	
occurrences (all)	7	0	
Conjunctivitis			
subjects affected / exposed	8 / 192 (4.17%)	6 / 84 (7.14%)	
occurrences (all)	9	7	

Oral candidiasis			
subjects affected / exposed	0 / 192 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	6	
Urinary tract infection			
subjects affected / exposed	14 / 192 (7.29%)	6 / 84 (7.14%)	
occurrences (all)	20	8	
Gastroenteritis			
subjects affected / exposed	10 / 192 (5.21%)	0 / 84 (0.00%)	
occurrences (all)	11	0	
Bronchitis			
subjects affected / exposed	10 / 192 (5.21%)	0 / 84 (0.00%)	
occurrences (all)	12	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	21 / 192 (10.94%)	12 / 84 (14.29%)	
occurrences (all)	26	18	
Hyperglycaemia			
subjects affected / exposed	14 / 192 (7.29%)	2 / 84 (2.38%)	
occurrences (all)	35	2	

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