Clinical trial results:
A Phase 3, Randomized, Open-label Study of NKTR-214 Combined with Nivolumab Versus Nivolumab in Participants with Previously Untreated Unresectable or Metastatic Melanoma

Summary

EudraCT number	2018-001423-40
Trial protocol	AT FR GB ES NL GR BE PL PT Outside EU/EEA SE FI IT RO
Global end of trial date	19 March 2024

Results information

Result version number	v1 (current)
This version publication date	04 April 2025
First version publication date	04 April 2025

Trial information

Trial identification

Sponsor protocol code	CA045-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@bms.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess efficacy of bempegaldesleukin combined with nivolumab and that of nivolumab monotherapy in participants with previously untreated 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 Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 75
Country: Number of subjects enrolled	Argentina: 35
Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Austria: 13
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 119
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Chile: 17
Country: Number of subjects enrolled	Czechia: 18
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 46
Country: Number of subjects enrolled	Germany: 79
Country: Number of subjects enrolled	Greece: 61
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 41
Country: Number of subjects enrolled	Mexico: 36
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Portugal: 13

Country: Number of subjects enrolled	Romania: 54
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Spain: 42
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Eswatini: 2
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	783
EEA total number of subjects	409

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)	458
From 65 to 84 years	325
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:
783 randomized and 770 treated

Period 1

Period 1 title	Pre-Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Bempegaldesleukin + Nivolumab

Arm description:
Bempegaldesleukin 0.006 mg/kg IV every 3 weeks + Nivolumab 360 mg IV every 3 weeks

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

Dosage and administration details:
360 mg every 3 weeks

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

Dosage and administration details:
0.006 mg/kg every 3 weeks

Arm title	Nivolumab

Arm description:
Nivolumab 360 mg IV every 3 weeks

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

Dosage and administration details:
360 mg every 3 weeks

Number of subjects in period 1	Bempegaldesleukin + Nivolumab	Nivolumab
Started	391	392
Completed	388	382
Not completed	3	10
Consent withdrawn by subject	-	7
Adverse Event unrelated to Study drug	2	1
Participant no longer meets study criteria	1	-
Other reasons	-	1
Disease Progression	-	1

Period 2	
Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Bempegaldesleukin + Nivolumab
Arm description: Bempegaldesleukin 0.006 mg/kg IV every 3 weeks + Nivolumab 360 mg IV every 3 weeks	
Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: 360 mg every 3 weeks	
Investigational medicinal product name	Bempegaldesleukin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: 0.006 mg/kg every 3 weeks	
Arm title	Nivolumab
Arm description: Nivolumab 360 mg IV every 3 weeks	
Arm type	Active comparator

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

Dosage and administration details:

360 mg every 3 weeks

Number of subjects in period 2	Bempegaldesleukin + Nivolumab	Nivolumab
Started	388	382
Completed	82	96
Not completed	306	286
Adverse event, serious fatal	3	5
Consent withdrawn by subject	3	5
Participant request to discontinue Study treatment	6	7
Study drug toxicity	35	36
Adverse Event unrelated to Study drug	15	15
Maximum clinical benefit	3	5
Participant no longer meets study criteria	1	4
Poor/Non-compliance	2	1
Other reasons	7	4
Lost to follow-up	-	1
Disease Progression	230	201
Administrative reason by the sponsor	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Bempegaldesleukin + Nivolumab
Reporting group description: Bempegaldesleukin 0.006 mg/kg IV every 3 weeks + Nivolumab 360 mg IV every 3 weeks	
Reporting group title	Nivolumab
Reporting group description: Nivolumab 360 mg IV every 3 weeks	

Reporting group values	Bempegaldesleukin + Nivolumab	Nivolumab	Total
Number of subjects	391	392	783
Age categorical Units:			
Age Continuous Units: years			
arithmetic mean	61.3	60.4	
standard deviation	± 13.2	± 13.5	-
Sex: Female, Male Units: Participants			
Female	162	163	325
Male	229	229	458
Race/Ethnicity, Customized Units: Subjects			
White	379	379	758
Black or African American	2	4	6
Asian	1	0	1
American Indian or Alaska Native	5	2	7
Other	4	7	11
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	81	73	154
Not Hispanic or Latino	165	153	318
Unknown or Not Reported	145	166	311

End points

End points reporting groups

Reporting group title	Bempegaldesleukin + Nivolumab
Reporting group description: Bempegaldesleukin 0.006 mg/kg IV every 3 weeks + Nivolumab 360 mg IV every 3 weeks	
Reporting group title	Nivolumab
Reporting group description: Nivolumab 360 mg IV every 3 weeks	
Reporting group title	Bempegaldesleukin + Nivolumab
Reporting group description: Bempegaldesleukin 0.006 mg/kg IV every 3 weeks + Nivolumab 360 mg IV every 3 weeks	
Reporting group title	Nivolumab
Reporting group description: Nivolumab 360 mg IV every 3 weeks	

Primary: Objective Response Rate (ORR) per Blinded Independent Central Review (BICR)

End point title	Objective Response Rate (ORR) per Blinded Independent Central Review (BICR)

End point description:

ORR is defined as the percentage of participants with a confirmed best overall response of complete response (CR) or partial response (PR) using RECIST v 1.1 per blinded independent central review (BICR) assessment. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

End point type	Primary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271	272		
Units: Percentage of participants				
number (confidence interval 95%)	27.7 (22.4 to 33.4)	36.0 (30.3 to 42.0)		

Statistical analyses

Statistical analysis title	Estimate of Odds Ratio (OR)

Statistical analysis description:

Bempegaldesleukin+Nivolumab over Nivolumab

Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab

Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0311
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Estimate of Odds Ratio (OR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.96

Primary: Progression-free Survival (PFS) per Blinded Independent Central Review (BICR)

End point title	Progression-free Survival (PFS) per Blinded Independent Central Review (BICR)

End point description:

PFS is defined as the time between the date of randomization and the first date of documented tumor progression using RECIST v 1.1 per blinded independent central review (BICR), or death due to any cause, whichever comes first. Progressive disease (PD)=At least a 20% increase in the sum of diameters of target lesions. The sum must also demonstrate an absolute increase of at least 5 mm.

End point type	Primary

End point timeframe:

From date of randomization to disease progression, or death, whichever comes first (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	392		
Units: Months				
median (confidence interval 95%)	4.17 (3.52 to 5.55)	4.99 (4.14 to 7.82)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	783
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3988 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.33

Notes:

[1] - Log-rank stratified 2-sided. Boundary for statistical significance p-value < 0.03

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time between the date of randomization and the date of death due to any cause. Participants who do not have a date of death will be censored on the last date for which a participant was known to be alive.

99999=NA

End point type	Primary

End point timeframe:

From date of randomization to date of death (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	392		
Units: Months				
median (confidence interval 95%)	29.67 (22.14 to 99999)	28.88 (21.32 to 99999)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	783
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6361
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.22

Secondary: Duration of Response (DoR) per Blinded Independent Central Review (BICR)

End point title	Duration of Response (DoR) per Blinded Independent Central Review (BICR)

End point description:

DOR is defined for participants who have a confirmed complete response (CR) or partial results (PR) as the date from first documented CR or PR using RECIST v 1.1 to the date of the documentation of disease progression per blinded independent central review (BICR) assessment or death due to any cause, whichever is earlier. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

99999=NA

End point type	Secondary

End point timeframe:

From date of randomization to disease progression, or death, whichever is earlier (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	98		
Units: Months				
median (confidence interval 95%)	29.67 (18.89 to 99999)	99999 (26.74 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Objective Response (TTR) per Blinded Independent Central Review (BICR)

End point title	Time to Objective Response (TTR) per Blinded Independent Central Review (BICR)

End point description:

Time to response (TTR) is defined for participants who had a confirmed complete response (CR) or partial response (PR) as the time from the date of randomization to date of first documented CR or PR per blinded independent central review (BICR) assessment using RECIST v 1.1. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	98		
Units: Months				
median (full range (min-max))	2.17 (1.0 to 15.3)	2.20 (1.2 to 15.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) per Blinded Independent Central Review (BICR)

End point title	Clinical Benefit Rate (CBR) per Blinded Independent Central Review (BICR)

End point description:

CBR, or equivalently the disease control rate (DCR) is defined as the percentage of participants with a best overall response of complete response (CR), partial response (PR), or stable disease (SD) as assessed by blinded independent central review (BICR) using RECIST v 1.1. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.SD=Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271	272		
Units: Percentage of participants				
number (confidence interval 95%)	56.1 (50.0 to 62.1)	58.5 (52.4 to 64.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) per Investigator

End point title	Objective Response Rate (ORR) per Investigator

End point description:

ORR is defined as the percentage of participants with a confirmed best overall response of complete response (CR) or partial response (PR) using RECIST v 1.1 per investigator assessment. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271	272		
Units: Percentage of participants				
number (confidence interval 95%)	29.2 (23.8 to 35.0)	36.4 (30.7 to 42.4)		

Statistical analyses

Statistical analysis title	Estimate of Odds Ratio (OR)

Statistical analysis description:

Bempegaldesleukin+Nivolumab over Nivolumab

Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0626
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Estimate of Odds Ratio (OR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.02

Secondary: Progression-free Survival (PFS) per Investigator

End point title	Progression-free Survival (PFS) per Investigator

End point description:

PFS is defined as the time between the date of randomization and the first date of documented tumor progression using RECIST v 1.1 per investigator, or death due to any cause, whichever comes first. Progressive disease (PD)=At least a 20% increase in the sum of diameters of target lesions. The sum must also demonstrate an absolute increase of at least 5 mm.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression, or death, whichever comes first (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	392		
Units: Months				
median (confidence interval 95%)	4.27 (4.04 to 6.14)	6.21 (4.60 to 10.25)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	783
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3713 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.33

Notes:

[2] - Log-rank stratified 2-sided. Boundary for statistical significance p-value < 0.03

Secondary: Objective Response Rate (ORR) per Blinded Independent Central Review (BICR) by Baseline PD-L1 Status

End point title	Objective Response Rate (ORR) per Blinded Independent Central Review (BICR) by Baseline PD-L1 Status

End point description:

ORR by baseline PD-L1 tumor cells expression (PD-L1 negative: <1%) vs. (PD-L1 positive: >=1%). ORR is defined as the percentage of participants with a confirmed best overall response of complete response (CR) or partial response (PR) using RECIST v 1.1 per blinded independent central review (BICR) assessment. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	248		
Units: Percentage of participants				
number (confidence interval 95%)				

Participants with baseline PD-L1 expression <1%	17.6 (10.8 to 26.4)	25.2 (17.3 to 34.6)		
Participants with baseline PD-L1 expression >=1%	36.4 (28.5 to 45.0)	47.5 (39.1 to 56.1)		

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Statistical analysis description: Bempegaldesleukin+Nivolumab vs. Nivolumab (PD-L1 Positive: >=1%)	
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9939
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.02

Statistical analysis title	Odds Ratio (OR)
Statistical analysis description: Bempegaldesleukin+Nivolumab vs. Nivolumab (PD-L1 Negative: <1%)	
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Odds ratio (OR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.24

Secondary: Time to Objective Response (TTR) per Investigator

End point title	Time to Objective Response (TTR) per Investigator

End point description:

Time to response (TTR) is defined for participants who had a confirmed complete response (CR) or partial response (PR) as the time from the date of randomization to date of first documented CR or PR per investigator assessment using RECIST v 1.1. CR=Disappearance of all target lesions. Any

pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	99		
Units: Months				
median (full range (min-max))	2.14 (1.6 to 18.3)	2.14 (1.8 to 12.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) per Investigator

End point title	Clinical Benefit Rate (CBR) per Investigator

End point description:

CBR, or equivalently the disease control rate (DCR) is defined as the percentage of participants with a best overall response of complete response (CR), partial response (PR), or stable disease (SD) as assessed by investigator using RECIST v 1.1. CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions. SD=Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271	272		
Units: Percentage of participants				
number (confidence interval 95%)	60.5 (54.4 to 66.4)	61.8 (55.7 to 67.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) per Investigator

End point title	Duration of Response (DoR) per Investigator

End point description:

DOR is defined for participants who have a confirmed complete response (CR) or partial results (PR) as the date from first documented CR or PR using RECIST v 1.1 to the date of the documentation of disease progression per investigator assessment or death due to any cause, whichever is earlier.
CR=Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. PR=At least a 30% decrease in the sum of diameters of target lesions.

99999=NA

End point type	Secondary

End point timeframe:

From date of randomization to disease progression, or death, whichever is earlier (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	99		
Units: Months				
median (confidence interval 95%)	99999 (17.31 to 99999)	99999 (21.68 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) per Blinded Independent Central Review (BICR) by baseline PD-L1 Status

End point title	Progression-free Survival (PFS) per Blinded Independent Central Review (BICR) by baseline PD-L1 Status

End point description:

PFS by baseline PD-L1 tumor cells expression (PD-L1 negative: <1%) vs. (PD-L1 positive: >=1%). PFS is defined as the time between the date of randomization and the first date of documented tumor progression using RECIST v 1.1 per blinded independent central review (BICR), or death due to any cause, whichever comes first. Progressive disease (PD)=At least a 20% increase in the sum of diameters of target lesions. The sum must also demonstrate an absolute increase of at least 5 mm.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression, or death, whichever comes first (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	357		
Units: Months				
median (confidence interval 95%)				

Participants with baseline PD-L1 expression <1%	3.25 (2.20 to 4.24)	2.30 (2.17 to 4.17)		
Participants with baseline PD-L1 expression >=1%	6.24 (4.47 to 10.45)	10.51 (6.05 to 28.88)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Bempegaldesleukin+Nivolumab vs. Nivo (PD-L1 positive: >=1%)	
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.51

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Bempegaldesleukin+Nivolumab vs. Nivo (PD-L1 negative: <1%)	
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.43

Secondary: Overall Survival (OS) by baseline PD-L1 Status

End point title	Overall Survival (OS) by baseline PD-L1 Status

End point description:

OS by baseline PD-L1 tumor cells expression (PD-L1 negative: <1%) vs. (PD-L1 positive: >=1%). OS is defined as the time between the date of randomization and the date of death due to any cause. Participants who do not have a date of death will be censored on the last date for which a participant was known to be alive.

99999=NA

End point type	Secondary

End point timeframe:

From date of randomization to date of death (Up to 37 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	357		
Units: Months				
median (confidence interval 95%)				
Participants with baseline PD-L1 expression <1%	21.16 (15.51 to 26.68)	21.13 (16.62 to 99999)		
Participants with baseline PD-L1 expression >=1%	99999 (29.67 to 99999)	99999 (28.88 to 99999)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Bempegaldesleukin+Nivolumab vs. Nivo (PD-L1 positive: >=1%)	
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.33

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Bempegaldesleukin+Nivolumab vs. Nivo (PD-L1 negative: <1%)	
Comparison groups	Bempegaldesleukin + Nivolumab v Nivolumab
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.4

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

Number of participants with any grade adverse events (AEs) including treatment-related AEs, AEs leading to discontinuation of any drug, serious adverse events (SAEs), treatment-related SAEs, and deaths from first dose to 30 days post last dose. An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose (Average of 11 months and a maximum up to 26 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	387	382		
Units: Participants				
AEs	378	364		
Drug-related AEs	351	281		
SAEs	132	130		
Drug-related SAEs	57	32		
AEs leading to discontinuation of any Drug	65	56		
Deaths	21	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with On-Treatment Laboratory Parameters that Worsened Relative to Baseline

End point title	Number of Participants with On-Treatment Laboratory Parameters that Worsened Relative to Baseline

End point description:

Number of participants with on-treatment laboratory parameters that worsened relative to baseline. Parameters include hematology, chemistry, liver function, and renal function using worst grade (grade 1-4 and grade 3-4) per national cancer institute (NCI) common terminology criteria for adverse events (CTCAE) v5 criteria.
Grade 1=Mild event
Grade 2=Moderate event

Grade 3=Severe event
Grade 4=Life threatening event

End point type	Secondary

End point timeframe:

From first dose to 100 days post last dose (Average of 13 months and a maximum up to 28 months)

End point values	Bempegaldesleukin + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	383	380		
Units: Participants				
Hemoglobin decreased grade 1-4	194	173		
Hemoglobin decreased grade 3-4	17	22		
Platelet count decreased grade 1-4	36	41		
Platelet count decreased grade 3-4	2	6		
Leukocytes decreased grade 1-4	29	46		
Leukocytes decreased grade 3-4	2	2		
Lymphocytes (absolute) decreased grade 1-4	304	194		
Lymphocytes (absolute) decreased grade 3-4	199	30		
Absolute Neutrophil count decreased grade 1-4	71	31		
Absolute Neutrophil, count decreased grade 3-4	8	2		
Neutrophils (absolute) decreased grade 1-4	57	29		
Neutrophils (absolute) decreased grade 3-4	10	2		
Alkaline Phosphatase increased grade 1-4	96	90		
Alkaline Phosphatase increased grade 3-4	2	6		
Aspartate Aminotransferase increased grade 1-4	96	115		
Aspartate Aminotransferase increased grade 3-4	9	17		
Alanine Aminotransferase increased grade 1-4	104	132		
Alanine Aminotransferase increased grade 3-4	11	13		
Bilirubin, total increased grade 1-4	36	46		
Bilirubin, total increased grade 3-4	2	4		
Creatinine increased grade 1-4	81	94		
Creatinine increased grade 3-4	2	6		
Amylase increased grade 1-4	51	78		
Amylase increased grade 3-4	3	6		
Lipase, total increased grade 1-4	90	126		
Lipase, total increased grade 3-4	17	17		
Hypernatremia grade 1-4	29	47		
Hypernatremia grade 3-4	2	0		
Hyponatremia grade 1-4	112	123		
Hyponatremia grade 3-4	6	11		

Hyperkalemia grade 1-4	91	85		
Hyperkalemia grade 3-4	9	6		
Hypokalemia grade 1-4	32	51		
Hypokalemia grade 3-4	5	2		
Hypercalcemia grade 1-4	45	45		
Hypercalcemia grade 3-4	1	0		
Hypocalcemia grade 1-4	78	82		
Hypocalcemia grade 3-4	5	0		
Hypoglycemia grade 1-4	42	39		
Hypoglycemia grade 3-4	3	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs are collected from first dose to 100 days post last dose (Average of 13 months and a maximum up to 28 months). Participants for deaths from their date of randomization to study completion date (Up to approximately 65 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Nivolumab

Reporting group description:

Nivolumab 360 mg IV every 3 weeks

Reporting group title	Bempegaldesleukin + Nivolumab

Reporting group description:

Bempegaldesleukin 0.006 mg/kg IV every 3 weeks + Nivolumab 360 mg IV every 3 weeks

Serious adverse events	Nivolumab	Bempegaldesleukin + Nivolumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	172 / 382 (45.03%)	161 / 388 (41.49%)	
number of deaths (all causes)	169	168	
number of deaths resulting from adverse events	56	54	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 382 (0.79%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	2 / 382 (0.52%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal metastasis			

subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	40 / 382 (10.47%)	37 / 388 (9.54%)	
occurrences causally related to treatment / all	0 / 42	0 / 40	
deaths causally related to treatment / all	0 / 32	0 / 31	
Malignant pleural effusion			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	3 / 382 (0.79%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to lymph nodes			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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			

subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oncologic complication			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm progression			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm malignant			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic neoplasm			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected neoplasm			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Ischaemia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	2 / 382 (0.52%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	1 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial occlusive disease			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			

subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Drowning			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Face oedema			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	4 / 382 (1.05%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	2 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 382 (0.79%)	4 / 388 (1.03%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 2	
Hanging			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Implant site haemorrhage			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised oedema			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 382 (1.05%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	1 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sudden death			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contrast media allergy			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytokine release syndrome			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular mass			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Alveolitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma-chronic obstructive pulmonary disease overlap syndrome			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune lung disease			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 382 (0.79%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 382 (0.52%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	1 / 382 (0.26%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epiglottic polyp			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal congestion			

subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 382 (0.26%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 382 (0.52%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pulmonary embolism			
subjects affected / exposed	2 / 382 (0.52%)	4 / 388 (1.03%)	
occurrences causally related to treatment / all	1 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	1 / 382 (0.26%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 382 (0.26%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	3 / 382 (0.79%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node palpable			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femoral neck fracture			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunisation reaction			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial tachycardia			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	4 / 382 (1.05%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopericarditis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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 ischaemia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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	3 / 382 (0.79%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			

subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 382 (0.26%)	7 / 388 (1.80%)	
occurrences causally related to treatment / all	0 / 1	5 / 7	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cerebrovascular disorder			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis autoimmune			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Haemorrhage intracranial			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	4 / 382 (1.05%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 382 (0.52%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	4 / 382 (1.05%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 382 (0.52%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node haemorrhage			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilia			

subjects affected / exposed	0 / 382 (0.00%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Uveitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Autoimmune colitis			
subjects affected / exposed	2 / 382 (0.52%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	0 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	3 / 382 (0.79%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	3 / 382 (0.79%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune pancreatitis			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 382 (0.52%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 382 (1.57%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	3 / 6	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated enterocolitis			
subjects affected / exposed	2 / 382 (0.52%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated pancreatitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	3 / 382 (0.79%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	1 / 3	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 382 (0.52%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cytolysis			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Hepatitis			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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			
Rash erythematous			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain of skin			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ingrowing nail			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated dermatitis			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hidradenitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoid-like reaction			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 382 (0.79%)	7 / 388 (1.80%)	
occurrences causally related to treatment / all	1 / 3	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune nephritis			
subjects affected / exposed	3 / 382 (0.79%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			

subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroiditis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Groin pain			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 382 (0.52%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	2 / 382 (0.52%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Morphoea			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 382 (0.52%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			

subjects affected / exposed	5 / 382 (1.31%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	4 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	3 / 382 (0.79%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	5 / 382 (1.31%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cellulitis			

subjects affected / exposed	1 / 382 (0.26%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis klebsiella			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (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	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	0 / 382 (0.00%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella urinary tract infection			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Orchitis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	8 / 382 (2.09%)	4 / 388 (1.03%)	
occurrences causally related to treatment / all	1 / 8	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	4 / 382 (1.05%)	5 / 388 (1.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 3	
Septic shock			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Severe acute respiratory syndrome			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin infection			
subjects affected / exposed	0 / 382 (0.00%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			

subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subcutaneous abscess			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis bacterial			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 382 (0.26%)	2 / 388 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	3 / 382 (0.79%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 382 (0.26%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hyponatraemia			
subjects affected / exposed	2 / 382 (0.52%)	3 / 388 (0.77%)	
occurrences causally related to treatment / all	1 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 382 (0.52%)	0 / 388 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 382 (0.00%)	1 / 388 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Nivolumab	Bempegaldesleukin + Nivolumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	336 / 382 (87.96%)	357 / 388 (92.01%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 382 (1.57%)	33 / 388 (8.51%)	
occurrences (all)	8	48	
Hypertension			
subjects affected / exposed	34 / 382 (8.90%)	27 / 388 (6.96%)	
occurrences (all)	53	39	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	39 / 382 (10.21%)	147 / 388 (37.89%)	
occurrences (all)	44	370	
Oedema peripheral			
subjects affected / exposed	30 / 382 (7.85%)	40 / 388 (10.31%)	
occurrences (all)	32	49	
Influenza like illness			
subjects affected / exposed	9 / 382 (2.36%)	71 / 388 (18.30%)	
occurrences (all)	11	235	
Fatigue			
subjects affected / exposed	104 / 382 (27.23%)	128 / 388 (32.99%)	
occurrences (all)	126	206	
Face oedema			
subjects affected / exposed	0 / 382 (0.00%)	20 / 388 (5.15%)	
occurrences (all)	0	38	
Chills			
subjects affected / exposed	5 / 382 (1.31%)	36 / 388 (9.28%)	
occurrences (all)	6	60	
Asthenia			
subjects affected / exposed	42 / 382 (10.99%)	68 / 388 (17.53%)	
occurrences (all)	46	116	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	45 / 382 (11.78%)	53 / 388 (13.66%)	
occurrences (all)	50	75	

Dyspnoea			
subjects affected / exposed	31 / 382 (8.12%)	31 / 388 (7.99%)	
occurrences (all)	38	37	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	24 / 382 (6.28%)	31 / 388 (7.99%)	
occurrences (all)	26	33	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	39 / 382 (10.21%)	31 / 388 (7.99%)	
occurrences (all)	52	32	
Amylase increased			
subjects affected / exposed	29 / 382 (7.59%)	20 / 388 (5.15%)	
occurrences (all)	55	27	
Aspartate aminotransferase increased			
subjects affected / exposed	34 / 382 (8.90%)	26 / 388 (6.70%)	
occurrences (all)	45	30	
Blood alkaline phosphatase increased			
subjects affected / exposed	20 / 382 (5.24%)	10 / 388 (2.58%)	
occurrences (all)	23	11	
Weight decreased			
subjects affected / exposed	22 / 382 (5.76%)	16 / 388 (4.12%)	
occurrences (all)	24	16	
Lipase increased			
subjects affected / exposed	37 / 382 (9.69%)	22 / 388 (5.67%)	
occurrences (all)	60	36	
Blood creatinine increased			
subjects affected / exposed	28 / 382 (7.33%)	20 / 388 (5.15%)	
occurrences (all)	36	23	
Blood creatine phosphokinase increased			
subjects affected / exposed	38 / 382 (9.95%)	23 / 388 (5.93%)	
occurrences (all)	57	29	
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	15 / 382 (3.93%)	48 / 388 (12.37%)	
occurrences (all)	19	77	
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 382 (5.24%)	38 / 388 (9.79%)	
occurrences (all)	22	45	
Headache			
subjects affected / exposed	56 / 382 (14.66%)	64 / 388 (16.49%)	
occurrences (all)	81	100	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	63 / 382 (16.49%)	61 / 388 (15.72%)	
occurrences (all)	74	68	
Eosinophilia			
subjects affected / exposed	7 / 382 (1.83%)	60 / 388 (15.46%)	
occurrences (all)	13	77	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	16 / 382 (4.19%)	29 / 388 (7.47%)	
occurrences (all)	18	35	
Abdominal pain			
subjects affected / exposed	34 / 382 (8.90%)	33 / 388 (8.51%)	
occurrences (all)	41	41	
Constipation			
subjects affected / exposed	51 / 382 (13.35%)	39 / 388 (10.05%)	
occurrences (all)	57	51	
Dry mouth			
subjects affected / exposed	13 / 382 (3.40%)	21 / 388 (5.41%)	
occurrences (all)	15	24	
Diarrhoea			
subjects affected / exposed	80 / 382 (20.94%)	96 / 388 (24.74%)	
occurrences (all)	113	166	
Vomiting			
subjects affected / exposed	37 / 382 (9.69%)	64 / 388 (16.49%)	
occurrences (all)	41	103	
Nausea			

subjects affected / exposed	67 / 382 (17.54%)	113 / 388 (29.12%)	
occurrences (all)	82	201	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	14 / 382 (3.66%)	30 / 388 (7.73%)	
occurrences (all)	14	31	
Erythema			
subjects affected / exposed	7 / 382 (1.83%)	28 / 388 (7.22%)	
occurrences (all)	8	37	
Pruritus			
subjects affected / exposed	80 / 382 (20.94%)	121 / 388 (31.19%)	
occurrences (all)	99	181	
Vitiligo			
subjects affected / exposed	34 / 382 (8.90%)	35 / 388 (9.02%)	
occurrences (all)	34	37	
Rash maculo-papular			
subjects affected / exposed	18 / 382 (4.71%)	30 / 388 (7.73%)	
occurrences (all)	25	42	
Rash			
subjects affected / exposed	63 / 382 (16.49%)	108 / 388 (27.84%)	
occurrences (all)	77	173	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	52 / 382 (13.61%)	74 / 388 (19.07%)	
occurrences (all)	54	78	
Hyperthyroidism			
subjects affected / exposed	28 / 382 (7.33%)	49 / 388 (12.63%)	
occurrences (all)	29	50	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	67 / 382 (17.54%)	99 / 388 (25.52%)	
occurrences (all)	88	183	
Back pain			
subjects affected / exposed	47 / 382 (12.30%)	35 / 388 (9.02%)	
occurrences (all)	54	47	
Myalgia			

subjects affected / exposed	28 / 382 (7.33%)	55 / 388 (14.18%)	
occurrences (all)	38	109	
Pain in extremity			
subjects affected / exposed	36 / 382 (9.42%)	34 / 388 (8.76%)	
occurrences (all)	42	44	
Infections and infestations			
COVID-19			
subjects affected / exposed	31 / 382 (8.12%)	32 / 388 (8.25%)	
occurrences (all)	33	33	
Upper respiratory tract infection			
subjects affected / exposed	20 / 382 (5.24%)	9 / 388 (2.32%)	
occurrences (all)	26	10	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	35 / 382 (9.16%)	68 / 388 (17.53%)	
occurrences (all)	39	86	
Hyponatraemia			
subjects affected / exposed	20 / 382 (5.24%)	15 / 388 (3.87%)	
occurrences (all)	26	16	
Hyperglycaemia			
subjects affected / exposed	28 / 382 (7.33%)	20 / 388 (5.15%)	
occurrences (all)	40	26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2020	statistical analysis for OS was updated
26 August 2021	Updated study treatment dose delay, resumption, and discontinuation
19 May 2022	treatment discontinuation update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported