Clinical trial results:
A Phase 2 Study of REGN2810, a Fully Human Monoclonal Antibody to Programmed Death-1, in Patients With Advanced Basal Cell Carcinoma Who Experienced Progression of Disease on Hedgehog Pathway Inhibitor Therapy, or Were Intolerant of Prior Hedgehog Pathway Inhibitor Therapy

Summary

EudraCT number	2016-003122-16
Trial protocol	BE DE AT GR ES FR IT
Global end of trial date	27 April 2023

Results information

Result version number	v1 (current)
This version publication date	09 May 2024
First version publication date	09 May 2024

Trial information

Trial identification

Sponsor protocol code	R2810-ONC-1620

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03132636
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.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	27 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to estimate the objective response rate (ORR) for metastatic Basal Cell Carcinoma (BCC) (group 1) and for unresectable locally advanced BCC (group 2) when treated with cemiplimab as a monotherapy

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study is conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 June 2017
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	Austria: 1
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	United States: 42
Worldwide total number of subjects	138
EEA total number of subjects	89

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)	58
From 65 to 84 years	68
85 years and over	12

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

138 participants were enrolled into 1 of 2 groups: (1) participants with metastatic Basal Cell Carcinoma (mBCC) or (2) with unresectable locally advanced BCC (laBCC) who experienced progression of disease on Hedgehog inhibitor (HHI) therapy, or response no better than stable disease for at least 9 mos. or were intolerant of prior HHI therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Metastatic BCC (mBCC)

Arm description:

Participants with metastatic BCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or CR.

Arm type	Experimental
Investigational medicinal product name	cemiplimab
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received open-label cemiplimab as an IV infusion over approximately 30 minutes

Arm title	Group 2: Unresectable Locally Advanced BCC (laBCC)

Arm description:

Participants with unresectable laBCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or confirmed CR.

Arm type	Experimental
Investigational medicinal product name	cemiplimab
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received open-label cemiplimab as an IV infusion over approximately 30 minutes

Number of subjects in period 1	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)
Started	54	84
Completed Treatment	11	28
Completed	6	19
Not completed	48	65
Adverse event, serious fatal	4	7
Physician decision	1	-
Subject decision	1	9
Withdrawal of consent	2	5
Sponsor decision	-	1
Non compliance with protocol by participant	1	1
Lost insurance coverage	1	-
Adverse event, non-fatal	1	2
Did not re-consent	1	-
Lost to follow-up	3	2
Progressive disease	33	36
Related to radiological outcomes	-	1
Unable to come to site for continued visits	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Metastatic BCC (mBCC)
Reporting group description:	
Participants with metastatic BCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or CR.	
Reporting group title	Group 2: Unresectable Locally Advanced BCC (laBCC)
Reporting group description:	
Participants with unresectable laBCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or confirmed CR.	

Reporting group values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)	Total
Number of subjects	54	84	138
Age categorical Units: Participants			
Adults (18-64 years)	27	31	58
From 65-74 years	18	19	37
75 years and over	9	34	43
Age Continuous Units: Years			
arithmetic mean	63.8	69.1	
standard deviation	± 11.09	± 12.84	-
Sex: Female, Male Units: Participants			
Female	16	28	44
Male	38	56	94
Race/Ethnicity, Customized Units: Subjects			
Race : White	47	57	104
Race : Not Reported	1	0	1
Race : Missing	6	27	33
Race/Ethnicity, Customized Units: Subjects			
Ethnicity : Not Hispanic or Latino	46	56	102
Ethnicity : Hispanic or Latino	2	1	3
Ethnicity : Missing	6	27	33

End points

End points reporting groups

Reporting group title	Group 1: Metastatic BCC (mBCC)

Reporting group description:

Participants with metastatic BCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or CR.

Reporting group title	Group 2: Unresectable Locally Advanced BCC (laBCC)

Reporting group description:

Participants with unresectable laBCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or confirmed CR.

Primary: Objective Response Rate (ORR) as assessed by Independent Central Review (ICR)

End point title	Objective Response Rate (ORR) as assessed by Independent Central Review (ICR)[1]

End point description:

ORR was defined as percentage of participants with best overall response of complete response (CR) or partial response (PR) according to RECIST v1.1 assessed as per ICR assessment. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<) 10 millimeter (mm) (< 1 centimeter [cm]). PR: At least a 30 percent (%) decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. ORR was determined by Clopper-Pearson method. Full analysis set (FAS) (included all enrolled participants for each group who passed screening and were deemed to be eligible for this study)

End point type	Primary

End point timeframe:

Up to 1422 days (approximately 46 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: ORR was determined by Clopper-Pearson method.

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Percentage of Participants				
number (confidence interval 95%)	22.2 (12.0 to 35.6)	32.1 (22.4 to 43.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) per Investigator assessment

End point title	Duration of Response (DOR) per Investigator assessment

End point description:

DOR per investigator assessment was determined for participants with best overall response of CR or PR. DOR was measured from the time measurement criteria are first met for CR/PR (whichever was first recorded) until the first date of recurrent or progressive disease (PD) (photographic or radiographic), or death due to any cause. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm (<1 cm). PR: At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. PD: At least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). DOR was determined by Kaplan-Meier estimate. "Number analyzed" signifies those participants with confirmed CR or PR.

End point type	Secondary

End point timeframe:

Up to 48 months

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	31		
Units: Months				
median (confidence interval 95%)	99999 (9.8 to 99999)	19.6 (16.7 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) per Investigator assessment

End point title	Objective Response Rate (ORR) per Investigator assessment

End point description:

ORR was defined as percentage of participants with best overall response of complete response (CR) or partial response (PR) according to RECIST v1.1 per Investigator assessment. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<) 10 millimeter (mm) (< 1 centimeter [cm]). PR: At least a 30 percent (%) decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. ORR was determined by Clopper-Pearson method. The FAS included all enrolled participants for each group who passed screening and were deemed to be eligible for this study.

End point type	Secondary

End point timeframe:

Up to 1422 days (approximately 46 months)

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Percentage of Participants				
number (confidence interval 95%)	25.9 (15.0 to 39.7)	36.9 (26.6 to 48.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as assessed by ICR

End point title	Duration of Response (DOR) as assessed by ICR

End point description:

DOR per ICR was determined for participants with best overall response of CR or PR. DOR measured from the time measurement criteria are first met for CR/PR (whichever was first recorded) until first date of recurrent or progressive disease (PD) (photographic or radiographic), or death due to any cause. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm (<1 cm). PR: At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. PD: At least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study (includes baseline sum if that is the smallest on study). DOR determined by Kaplan-Meier estimate. FAS included all enrolled participants for each group who passed screening and were deemed eligible; "Number analyzed" signifies those participants with confirmed CR or PR.

End point type	Secondary

End point timeframe:

Up to 48 months

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	27		
Units: Months				
median (confidence interval 95%)	99999 (9.8 to 99999)	99999 (15.5 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response (CR) Rate as assessed by ICR

End point title	Complete Response (CR) Rate as assessed by ICR

End point description:

CR rate was determined by the percentage of participants with best overall response of CR. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm (<1 cm). CR rate 95% confidence interval determined by Clopper-Pearson exact confidence interval. The FAS included all enrolled participants for each group who passed screening and were deemed to be eligible for this study.

End point type	Secondary

End point timeframe:

Up to 48 months

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Percentage of Participants				
number (confidence interval 95%)	3.7 (0.5 to 12.7)	8.3 (3.4 to 16.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response (CR) Rate per Investigator assessment

End point title	Complete Response (CR) Rate per Investigator assessment

End point description:

CR rate was determined by the percentage of participants with best overall response of CR. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm (<1 cm). CR rate 95% confidence interval determined by Clopper-Pearson exact confidence interval. The FAS included all enrolled participants for each group who passed screening and were deemed to be eligible for this study.

End point type	Secondary

End point timeframe:

From date of treatment until best objective response of CR, up to 60 months (approximately 260 weeks)

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Percentage of Participants				
number (confidence interval 95%)	3.7 (0.5 to 12.7)	8.3 (3.4 to 16.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) as assessed by ICR

End point title	Progression Free Survival (PFS) as assessed by ICR

End point description:

PFS was defined as the time from start of treatment until the first date of recurrent or PD (photographic or radiographic), or death due to any cause, whichever occurred first, was determined by IRC. PD: At least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). PFS was determined by Kaplan-Meier estimate. FAS (all enrolled participants for each group who passed screening and were deemed to be eligible for this study)

End point type	Secondary

End point timeframe:

Up to 60 months

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Months				
median (confidence interval 95%)	10.1 (4.2 to 15.9)	16.5 (8.6 to 21.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) per Investigator assessment

End point title	Progression Free Survival (PFS) per Investigator assessment

End point description:

PFS was defined as the time from start of treatment until the first date of recurrent or PD (photographic or radiographic), or death due to any cause, whichever occurred first, was determined by IRC. PD: At least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). PFS was determined by Kaplan-Meier estimate. The FAS included all enrolled participants for each group who passed screening and were deemed to be eligible for this study.

End point type	Secondary

End point timeframe:

Up to 60 months

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Months				
median (confidence interval 95%)	6.6 (4.2 to 8.3)	18.1 (10.4 to 21.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was measured as time from the start of treatment until death due to any cause. Participants who did not die were censored at the last date that participant was documented to be alive. OS was calculated based on Kaplan-Meier estimate. The FAS included all enrolled participants for each group who passed screening and were deemed to be eligible for this study.

End point type	Secondary

End point timeframe:

Up to 60 months

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Months				
median (confidence interval 95%)	49.9 (28.4 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Patient-reported Outcomes in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)

End point title	Change from Baseline of Patient-reported Outcomes in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)

End point description:

EORTC QLQ-C30: a 30-item questionnaire used to assess overall QoL in cancer patients & consists of 15 domains: 1 Global Health Status (GHS)/QoL scale, 5 functional scales (Physical, role, cognitive, emotional, social), 9 symptom scales/items (Fatigue, nausea & vomiting, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, financial impact). Most items scored 1 ("not at all") - 4 ("very much") except items contributing to GHS/QoL (scored 1 ("very poor") - 7 ("excellent"). Linear transformation applied to raw scores (all transformed scores lie between 0-100). For GHS/QoL & 5 functional scales: higher score indicates "better" quality of life/functioning & a positive change from baseline indicates improvement. Symptom scales/items: higher score indicates a "worse" level of symptoms/problems, negative change from baseline indicates improvement. Number ("n") signifies those participants who were evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 2 to 9 (C2D1, C3D1, C4D1, C5D1, C6D1, C7D1, C8D1, C9D1) (Cycles 1-5 [Each cycle of 9 weeks], Cycles 6 to 9 [Each cycle of 12 weeks])

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Physical Functioning: Change at C2D1 (n=43; n=75)	-4.88 (± 14.274)	-1.55 (± 12.101)		
Physical Functioning: Change at C3D1 (n=29; n=65)	-1.78 (± 13.481)	-0.56 (± 15.947)		
Physical Functioning: Change at C4D1 (n=26; n=55)	-6.60 (± 12.828)	-3.79 (± 17.814)		
Physical Functioning: Change at C5D1 (n=20; n=50)	1.08 (± 10.033)	-2.86 (± 17.063)		
Physical Functioning: Change at C6D1 (n=19; n=40)	-1.67 (± 9.734)	0.33 (± 12.073)		
Physical Functioning: Change at C7D1 (n=13; n=33)	-0.38 (± 11.142)	-0.20 (± 15.410)		
Physical Functioning: Change at C8D1 (n=10; n=33)	-1.33 (± 12.090)	-3.03 (± 13.549)		
Physical Functioning: Change at C9D1 (n=11; n=29)	-2.27 (± 8.765)	-5.06 (± 20.444)		
Role Functioning: Change at C2D1 (n=54; n=84)	-2.71 (± 27.442)	-3.11 (± 20.264)		
Role Functioning: Change at C3D1 (n=29; n=65)	5.17 (± 27.854)	-4.87 (± 25.297)		
Role Functioning: Change at C4D1 (n=26; n=55)	-3.21 (± 25.394)	-6.06 (± 26.326)		
Role Functioning: Change at C5D1 (n=20; n=50)	5.00 (± 22.361)	-5.33 (± 26.393)		
Role Functioning: Change at C6D1 (n=19; n=40)	6.14 (± 21.667)	-3.33 (± 16.963)		
Role Functioning: Change at C7D1 (n=13; n=33)	12.82 (± 24.677)	-7.07 (± 16.682)		
Role Functioning: Change at C8D1 (n=10; n=33)	15.00 (± 25.398)	-4.04 (± 19.557)		

Role Functioning: Change at C9D1 (n=11; n=29)	9.09 (± 22.808)	-9.77 (± 30.052)		
Emotional Functioning: Change at C2D1 (n=54; n=74)	3.17 (± 19.638)	1.95 (± 20.483)		
Emotional Functioning: Change at C3D1 (n=29; n=64)	1.15 (± 18.730)	1.56 (± 18.538)		
Emotional Functioning: Change at C4D1 (n=26; n=54)	3.53 (± 22.007)	1.39 (± 21.277)		
Emotional Functioning: Change at C5D1 (n=20; n=49)	5.83 (± 24.046)	-4.59 (± 19.622)		
Emotional Functioning: Change at C6D1 (n=19; n=40)	7.02 (± 20.650)	1.04 (± 19.809)		
Emotional Functioning: Change at C7D1 (n=13; n=33)	3.85 (± 18.199)	-4.63 (± 19.576)		
Emotional Functioning: Change at C8D1 (n=11; n=33)	16.67 (± 25.000)	3.11 (± 19.810)		
Emotional Functioning: Change at C9D1 (n=11; n=29)	5.30 (± 17.189)	2.11 (± 17.246)		
Cognitive Functioning: Change at C2D1 (n=54; n=74)	0.78 (± 13.586)	-2.48 (± 26.985)		
Cognitive Functioning: Change at C3D1 (n=29; n=64)	-1.72 (± 16.871)	-4.17 (± 23.382)		
Cognitive Functioning: Change at C4D1 (n=26; n=54)	-0.64 (± 15.261)	-4.94 (± 21.385)		
Cognitive Functioning: Change at C5D1 (n=20; n=49)	-4.17 (± 14.178)	-6.46 (± 25.188)		
Cognitive Functioning: Change at C6D1 (n=19; n=40)	-0.88 (± 12.998)	-1.25 (± 19.017)		
Cognitive Functioning: Change at C7D1 (n=13; n=33)	-2.56 (± 11.479)	-5.56 (± 18.942)		
Cognitive Functioning: Change at C8D1 (n=11; n=33)	-6.06 (± 11.237)	1.52 (± 17.362)		
Cognitive Functioning: Change at C9D1 (n=11; n=29)	-10.61 (± 25.025)	-2.30 (± 23.873)		
Social Functioning: Change at C2D1 (n=54; n=74)	0.39 (± 19.412)	4.50 (± 21.422)		
Social Functioning: Change at C3D1 (n=29; n=64)	3.45 (± 16.891)	0.78 (± 21.088)		
Social Functioning: Change at C4D1 (n=26; n=54)	3.85 (± 24.179)	1.85 (± 23.272)		
Social Functioning: Change at C5D1 (n=20; n=49)	3.33 (± 22.685)	0.34 (± 23.445)		
Social Functioning: Change at C6D1 (n=19; n=40)	10.53 (± 16.860)	0.00 (± 24.749)		
Social Functioning: Change at C7D1 (n=13; n=33)	12.82 (± 22.724)	0.00 (± 18.162)		
Social Functioning: Change at C8D1 (n=11; n=33)	10.61 (± 15.407)	2.02 (± 23.848)		
Social Functioning: Change at C9D1 (n=11; n=29)	9.09 (± 13.670)	-2.30 (± 27.359)		
Fatigue: Change at C2D1 (n=54; n=84)	5.17 (± 22.919)	6.44 (± 24.542)		
Fatigue: Change at C3D1 (n=29; n=65)	1.92 (± 18.322)	6.58 (± 24.901)		
Fatigue: Change at C4D1 (n=26; n=55)	-2.56 (± 21.154)	7.58 (± 25.912)		
Fatigue: Change at C5D1 (n=20; n=50)	-5.56 (± 24.048)	9.67 (± 23.404)		
Fatigue: Change at C6D1 (n=19; n=40)	-5.85 (± 19.376)	7.78 (± 17.649)		
Fatigue: Change at C7D1 (n=13; n=33)	-1.71 (± 19.692)	14.14 (± 20.838)		

Fatigue: Change at C8D1 (n=10; n=33)	-7.78 (± 24.595)	9.09 (± 19.534)		
Fatigue: Change at C9D1 (n=11; n=29)	-1.01 (± 16.607)	12.64 (± 20.080)		
Nausea/Vomiting: Change at C2D1 (n=54, n=84)	-0.78 (± 8.095)	0.22 (± 12.703)		
Nausea/Vomiting: Change at C3D1 (n=29, n=65)	0.00 (± 13.363)	-1.79 (± 12.884)		
Nausea/Vomiting: Change at C4D1 (n=26, n=55)	0.00 (± 16.330)	0.30 (± 13.414)		
Nausea/Vomiting: Change at C5D1 (n=20, n=50)	0.83 (± 10.080)	1.00 (± 13.640)		
Nausea/Vomiting: Change at C6D1 (n=19, n=40)	-0.88 (± 3.824)	1.67 (± 13.503)		
Nausea/Vomiting: Change at C7D1 (n=13, n=33)	-1.28 (± 14.372)	3.03 (± 13.472)		
Nausea/Vomiting: Change at C8D1 (n=10, n=33)	0.00 (± 0.000)	0.51 (± 12.832)		
Nausea/Vomiting: Change at C9D1 (n=11, n=29)	0.00 (± 0.000)	-2.30 (± 13.890)		
Pain: Change at C2D1 (n=54, n=84)	-2.33 (± 30.338)	-0.22 (± 26.351)		
Pain: Change at C3D1 (n=29, n=65)	-9.77 (± 22.056)	-1.54 (± 30.151)		
Pain: Change at C4D1 (n=26, n=55)	0.00 (± 29.439)	-4.85 (± 25.795)		
Pain: Change at C5D1 (n=20, n=50)	-4.17 (± 25.291)	-4.00 (± 25.098)		
Pain: Change at C6D1 (n=19, n=40)	-14.04 (± 29.535)	-2.92 (± 24.427)		
Pain: Change at C7D1 (n=13, n=33)	-21.79 (± 29.174)	-4.04 (± 24.661)		
Pain: Change at C8D1 (n=11, n=33)	-13.64 (± 25.624)	-7.58 (± 25.716)		
Pain: Change at C9D1 (n=11, n=29)	-19.70 (± 27.707)	-5.17 (± 24.030)		
Dyspnoea: Change at C2D1 (n=42, n=84)	2.38 (± 17.097)	1.33 (± 24.162)		
Dyspnoea: Change at C3D1 (n=28, n=65)	3.57 (± 16.578)	-0.51 (± 23.930)		
Dyspnoea: Change at C4D1 (n=25, n=55)	0.00 (± 16.667)	2.42 (± 24.724)		
Dyspnoea: Change at C5D1 (n=19, n=49)	3.51 (± 21.928)	0.00 (± 28.054)		
Dyspnoea: Change at C6D1 (n=18, n=40)	1.85 (± 13.873)	-1.67 (± 19.900)		
Dyspnoea: Change at C7D1 (n=12, n=33)	2.78 (± 30.011)	2.02 (± 21.952)		
Dyspnoea: Change at C8D1 (n=10, n=33)	16.67 (± 36.004)	2.02 (± 21.952)		
Dyspnoea: Change at C9D1 (n=10, n=29)	6.67 (± 26.294)	2.30 (± 17.663)		
Insomnia: Change at C2D1 (n=54, n=84)	-2.33 (± 26.622)	0.44 (± 24.195)		
Insomnia: Change at C3D1 (n=29, n=65)	-6.90 (± 24.200)	-0.51 (± 26.016)		
Insomnia: Change at C4D1 (n=26, n=55)	-10.26 (± 29.468)	-1.82 (± 19.687)		
Insomnia: Change at C5D1 (n=20, n=50)	-15.00 (± 31.484)	1.33 (± 30.087)		
Insomnia: Change at C6D1 (n=19, n=40)	-17.54 (± 32.142)	-4.17 (± 24.093)		

Insomnia: Change at C7D1 (n=13, n=33)	-7.69 (± 41.172)	1.01 (± 28.241)		
Insomnia: Change at C8D1 (n=10, n=33)	-13.33 (± 54.885)	3.03 (± 25.500)		
Insomnia: Change at C9D1 (n=11, n=29)	-6.06 (± 38.925)	5.75 (± 25.306)		
Appetite loss: Change at C2D1 (n=54, n=74)	4.65 (± 26.807)	-2.25 (± 27.215)		
Appetite loss: Change at C3D1 (n=29, n=62)	-2.30 (± 15.252)	-4.30 (± 22.163)		
Appetite loss: Change at C4D1 (n=26, n=54)	-1.28 (± 30.523)	-3.09 (± 26.117)		
Appetite loss: Change at C5D1 (n=20, n=49)	3.33 (± 21.357)	-1.36 (± 30.398)		
Appetite loss: Change at C6D1 (n=19, n=39)	-1.75 (± 17.476)	-2.56 (± 29.004)		
Appetite loss: Change at C7D1 (n=13, n=33)	-5.13 (± 12.518)	-1.01 (± 30.601)		
Appetite loss: Change at C8D1 (n=10, n=32)	-3.33 (± 10.541)	-2.08 (± 31.609)		
Appetite loss: Change at C9D1 (n=11, n=28)	-3.03 (± 17.979)	1.19 (± 30.741)		
Constipation: Change at C2D1 (n=54, n=74)	1.55 (± 19.181)	2.25 (± 21.603)		
Constipation: Change at C3D1 (n=29, n=63)	0.00 (± 21.822)	1.06 (± 20.712)		
Constipation: Change at C4D1 (n=26, n=54)	-2.56 (± 18.674)	1.23 (± 21.440)		
Constipation: Change at C5D1 (n=20, n=49)	5.00 (± 16.312)	-0.68 (± 22.037)		
Constipation: Change at C6D1 (n=19, n=40)	0.00 (± 15.713)	-1.67 (± 18.413)		
Constipation: Change at C7D1 (n=13, n=33)	5.13 (± 18.490)	4.04 (± 13.838)		
Constipation: Change at C8D1 (n=10, n=33)	13.33 (± 23.307)	-2.02 (± 16.540)		
Constipation: Change at C9D1 (n=11, n=29)	0.00 (± 14.907)	1.15 (± 22.683)		
Diarhoea: Change at C2D1 (n=54, n=74)	3.88 (± 14.924)	0.45 (± 24.360)		
Diarhoea: Change at C3D1 (n=29, n=64)	1.15 (± 14.037)	-1.04 (± 20.547)		
Diarhoea: Change at C4D1 (n=26, n=54)	3.85 (± 23.715)	-1.85 (± 19.870)		
Diarhoea: Change at C5D1 (n=20, n=49)	6.67 (± 20.520)	-0.68 (± 23.064)		
Diarhoea: Change at C6D1 (n=19, n=40)	3.51 (± 18.904)	-1.67 (± 18.413)		
Diarhoea: Change at C7D1 (n=13, n=33)	0.00 (± 13.608)	1.01 (± 19.516)		
Diarhoea: Change at C8D1 (n=11, n=33)	0.00 (± 14.907)	-1.01 (± 19.516)		
Diarhoea: Change at C9D1 (n=11, n=29)	0.00 (± 14.907)	-2.30 (± 21.696)		
Financial Problems: Change at C2D1 (n=54, n=74)	-3.10 (± 17.539)	-3.15 (± 25.385)		
Financial Problems: Change at C3D1 (n=28, n=63)	0.00 (± 18.144)	-4.23 (± 24.313)		
Financial Problems: Change at C4D1 (n=26, n=54)	-5.13 (± 22.494)	-4.94 (± 23.710)		
Financial Problems: Change at C5D1 (n=20, n=49)	0.00 (± 18.732)	-6.80 (± 22.546)		

Financial Problems: Change at C6D1 (n=19, n=40)	-1.75 (± 23.501)	-5.83 (± 27.099)		
Financial Problems: Change at C7D1 (n=13, n=33)	-2.56 (± 21.350)	1.01 (± 19.516)		
Financial Problems: Change at C8D1 (n=11, n=33)	-3.03 (± 17.979)	1.01 (± 19.516)		
Financial Problems: Change at C9D1 (n=11, n=29)	-6.06 (± 20.101)	-2.30 (± 23.454)		
Global health status: Change at C2D1 (n=54, n=72)	-3.68 (± 21.845)	2.55 (± 15.298)		
Global health status: Change at C3D1 (n=29, n=62)	3.74 (± 14.362)	-2.55 (± 19.823)		
Global health status: Change at C4D1 (n=26, n=51)	-2.24 (± 14.636)	-0.49 (± 18.136)		
Global health status: Change at C5D1 (n=20, n=48)	7.50 (± 14.023)	-1.91 (± 21.210)		
Global health status: Change at C6D1 (n=19, n=38)	10.96 (± 11.802)	4.17 (± 19.447)		
Global health status: Change at C7D1 (n=13, n=32)	16.03 (± 22.428)	-3.13 (± 19.715)		
Global health status: Change at C8D1 (n=11, n=31)	9.09 (± 13.670)	2.15 (± 21.727)		
Global health status: Change at C9D1 (n=11, n=28)	8.33 (± 20.412)	-7.14 (± 28.211)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Patient-reported Outcomes in Skindex-16 Questionnaire

End point title	Change from Baseline of Patient-reported Outcomes in Skindex-16 Questionnaire

End point description:

Skindex-16 questionnaire: 16 questions related to quality of life in cancer patients. Each item is rated on a 7-point Likert scale (0=never bothered - 6=always bothered). Each raw score is multiplied by 16.667 to transform all responses to a linear scale from 0 (no effect) to 100 (effect experienced all the time). Responses are categorized into 3 subscales: symptom, emotional & functional; respective scores are expressed in a linear scale from 0 to 100. Symptoms scale score is an average of items 1 - 4 expressed in a linear scale from 0 - 100, Emotions scale score is an average of items 5 - 11 expressed in a linear scale from 0 - 100 & Functioning scale score is an average of items 12 - 16 expressed in a linear scale from 0 - 100. A negative change from baseline indicates an improvement compared to baseline. FAS (all enrolled participants); Number ("n") signifies those participants who were evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 2 to 9 (Cycles 1-5 [Each cycle of 9 weeks], Cycles 6 to 9 [Each cycle of 12 weeks])

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Emotions: Change at C2D1 (n=42, n=69)	-6.90 (± 24.422)	-8.93 (± 27.767)		
Emotions: Change at C3D1 (n=26, n=63)	-7.92 (± 18.033)	-8.60 (± 25.641)		
Emotions: Change at C4D1 (n=22, n=51)	-3.97 (± 17.175)	-11.45 (± 24.215)		
Emotions: Change at C5D1 (n=17, n=46)	-0.14 (± 12.835)	-10.25 (± 24.646)		
Emotions: Change at C6D1 (n=16, n=35)	-9.08 (± 22.824)	-19.73 (± 27.304)		
Emotions: Change at C7D1 (n=12, n=30)	6.55 (± 17.053)	-13.65 (± 27.132)		
Emotions: Change at C8D1 (n=10, n=30)	-0.71 (± 8.478)	-13.97 (± 25.001)		
Emotions: Change at C9D1 (n=11, n=28)	5.70 (± 14.711)	-15.08 (± 31.843)		
Symptoms: Change at C2D1 (n=54, n=84)	0.99 (± 18.788)	-1.31 (± 21.607)		
Symptoms: Change at C3D1 (n=26, n=64)	3.85 (± 16.580)	-0.26 (± 24.158)		
Symptoms: Change at C4D1 (n=22, n=52)	5.30 (± 18.464)	-6.62 (± 23.917)		
Symptoms: Change at C5D1 (n=17, n=47)	-0.98 (± 15.205)	-4.11 (± 18.062)		
Symptoms: Change at C6D1 (n=16, n=36)	-1.56 (± 16.307)	-1.85 (± 21.419)		
Symptoms: Change at C7D1 (n=12, n=30)	4.17 (± 23.233)	0.69 (± 24.518)		
Symptoms: Change at C8D1 (n=10, n=31)	5.00 (± 17.213)	-2.96 (± 24.395)		
Symptoms: Change at C9D1 (n=11, n=28)	8.33 (± 21.246)	-3.42 (± 24.455)		
Functioning: Change at C2D1 (n=54, n=84)	-3.49 (± 19.183)	-4.98 (± 23.650)		
Functioning: Change at C3D1 (n=26, n=63)	-5.00 (± 18.166)	-4.76 (± 20.203)		
Functioning: Change at C4D1 (n=22, n=51)	-8.18 (± 24.119)	-5.82 (± 23.275)		
Functioning: Change at C5D1 (n=17, n=47)	-7.06 (± 20.746)	-3.76 (± 16.369)		
Functioning: Change at C6D1 (n=16, n=35)	-12.08 (± 27.022)	-11.14 (± 18.113)		
Functioning: Change at C7D1 (n=12, n=30)	-3.89 (± 19.583)	-6.00 (± 15.767)		
Functioning: Change at C8D1 (n=10, n=30)	-7.33 (± 23.402)	-7.00 (± 17.926)		
Functioning: Change at C9D1 (n=11, n=28)	-9.39 (± 21.072)	-5.60 (± 20.965)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration at Pre-infusion (Ctrough)

End point title	Serum Concentration at Pre-infusion (Ctrough)

End point description:

Ctrough of cemiplimab was reported; Pharmacokinetic (PK) analysis set (included all participants who received any cemiplimab and had at least one non-missing post-baseline measurement of cemiplimab concentration in serum); Number ("n") signifies those participants who were evaluable at specific time points.

End point type	Secondary

End point timeframe:

At pre-infusion on Cycle 1 Day 22 and Cycle 3 Day 1 (Each cycle of 9 weeks)

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Milligram per Liter (mg/L)				
arithmetic mean (standard deviation)				
Cycle 1 Day 22 (n=50, n=78)	28.3 (± 18.4)	29.8 (± 12.0)		
Cycle 3 Day 1 (n=32, n=66)	60.6 (± 28.2)	68.6 (± 32.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. TEAEs are defined as AEs that developed or worsened during the on-treatment period and treatment-related AEs that occur during post-treatment period. A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in any of the following outcomes: death, life-threatening, required initial or prolonged in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. Any TEAE included participants with both serious and non-serious TEAEs. The safety analysis set (SAF) included all enrolled participants who received any study drug for each group.

End point type	Secondary

End point timeframe:

Up to 1422 days (approximately 46 months)

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: Participants				
Participants with any TEAEs	51	83		
Participants with any Serious TEAEs	16	31		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibody (ADA) Status

End point title	Number of Participants With Anti-Drug Antibody (ADA) Status

End point description:

Immunogenicity was characterized by ADA responses & titers. Responses categories: Negative - ADA negative response at all time points, regardless of missing samples; Pre-existing immunoreactivity - ADA positive response at baseline with all post first dose negative results or positive response at baseline with all post first dose ADA responses < 9-fold over baseline titer levels; Treatment-boosted response - positive response in the assay post first dose, ≥ 9-fold over baseline titer levels, when baseline results are positive; Treatment-emergent response - ADA positive response in the cemiplimab ADA assay post first dose when baseline results = negative or missing. The anti-drug antibody set included all participants who received cemiplimab and who had at least 1 non-missing result in the ADA assay after the first dose of the study drug.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 43; Cycles 3 and 5: Day 1 (Each cycle of 9 weeks)

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	81		
Units: Participants				
Negative ADA	50	74		
Pre-Existing ADA	2	2		
Treatment-emergent ADA	0	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration at End of Infusion (Cmax)

End point title	Serum Concentration at End of Infusion (Cmax)

End point description:

Cmax of cemiplimab was reported; PK analysis set (included all participants who received any cemiplimab and had at least one non-missing post-baseline measurement of cemiplimab concentration in serum); Number ("n") signifies those participants who were evaluable at specific time points

End point type	Secondary

End point timeframe:

At end-of-infusion (within 10 minutes after the end of infusion) on Cycle 1 Day 1 and Cycle 3 Day 1 (Each cycle of 9 weeks)

End point values	Group 1: Metastatic BCC (mBCC)	Group 2: Unresectable Locally Advanced BCC (laBCC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	84		
Units: mg/L				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=47, n=81)	103 (± 25.2)	104 (± 45.5)		
Cycle 3 Day 1 (n=54, n=84)	160 (± 52.7)	192 (± 91.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse events (AEs) were collected from the time of informed consent signature until 105 days after the last dose of study drug (up to 2129 days)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Group 2: Unresectable Locally Advanced BCC (laBCC)

Reporting group description:

Participants with unresectable laBCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or confirmed CR.

Reporting group title	Group 1: Metastatic BCC (mBCC)

Reporting group description:

Participants with metastatic BCC received IV infusion of cemiplimab at a dose of 350 mg Q3W for up to 93 weeks of treatment cycles (cycles 1-5 [each cycle of 9 weeks] followed by cycles 6-9 [each cycle of 12 weeks]) or until PD, unacceptable toxicity, withdrawal of consent, or CR.

Serious adverse events	Group 2: Unresectable Locally Advanced BCC (laBCC)	Group 1: Metastatic BCC (mBCC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 84 (39.29%)	18 / 54 (33.33%)	
number of deaths (all causes)	21	22	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm malignant			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infected neoplasm			
subjects affected / exposed	2 / 84 (2.38%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoproliferative disorder			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural effusion			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary embolism			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (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			
Tibia fracture			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			

subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radial head dislocation			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haemorrhage			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
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	0 / 84 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune myocarditis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune pericarditis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated myocarditis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 84 (2.38%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	1 / 84 (1.19%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (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 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	2 / 84 (2.38%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Ear disorder			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	2 / 84 (2.38%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (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	1 / 84 (1.19%)	0 / 54 (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	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune hepatitis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermal cyst			

subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 84 (2.38%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 84 (2.38%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Dupuytren's contracture			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Oral candidiasis			

subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 84 (4.76%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin infection			

subjects affected / exposed	0 / 84 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cachexia			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Group 2: Unresectable Locally Advanced BCC (laBCC)	Group 1: Metastatic BCC (mBCC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 84 (90.48%)	50 / 54 (92.59%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	5 / 84 (5.95%)	1 / 54 (1.85%)	
occurrences (all)	5	1	
Basal cell carcinoma			
subjects affected / exposed	8 / 84 (9.52%)	3 / 54 (5.56%)	
occurrences (all)	9	5	
Tumour haemorrhage			
subjects affected / exposed	9 / 84 (10.71%)	1 / 54 (1.85%)	
occurrences (all)	12	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 84 (10.71%)	12 / 54 (22.22%)	
occurrences (all)	15	33	
General disorders and administration site conditions			

Influenza like illness			
subjects affected / exposed	5 / 84 (5.95%)	2 / 54 (3.70%)	
occurrences (all)	7	2	
Fatigue			
subjects affected / exposed	25 / 84 (29.76%)	24 / 54 (44.44%)	
occurrences (all)	35	32	
Pain			
subjects affected / exposed	2 / 84 (2.38%)	3 / 54 (5.56%)	
occurrences (all)	2	4	
Pyrexia			
subjects affected / exposed	5 / 84 (5.95%)	7 / 54 (12.96%)	
occurrences (all)	7	9	
Oedema peripheral			
subjects affected / exposed	5 / 84 (5.95%)	7 / 54 (12.96%)	
occurrences (all)	5	9	
Asthenia			
subjects affected / exposed	17 / 84 (20.24%)	5 / 54 (9.26%)	
occurrences (all)	27	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 84 (11.90%)	4 / 54 (7.41%)	
occurrences (all)	14	5	
Dyspnoea			
subjects affected / exposed	11 / 84 (13.10%)	4 / 54 (7.41%)	
occurrences (all)	18	5	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 84 (3.57%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Investigations			
Weight increased			
subjects affected / exposed	2 / 84 (2.38%)	8 / 54 (14.81%)	
occurrences (all)	2	12	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 84 (4.76%)	3 / 54 (5.56%)	
occurrences (all)	6	3	

Blood creatinine increased			
subjects affected / exposed	8 / 84 (9.52%)	4 / 54 (7.41%)	
occurrences (all)	9	4	
Weight decreased			
subjects affected / exposed	7 / 84 (8.33%)	5 / 54 (9.26%)	
occurrences (all)	7	6	
Blood creatine phosphokinase increased			
subjects affected / exposed	6 / 84 (7.14%)	4 / 54 (7.41%)	
occurrences (all)	8	5	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 84 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Fall			
subjects affected / exposed	5 / 84 (5.95%)	4 / 54 (7.41%)	
occurrences (all)	5	7	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 84 (14.29%)	7 / 54 (12.96%)	
occurrences (all)	14	8	
Paraesthesia			
subjects affected / exposed	4 / 84 (4.76%)	3 / 54 (5.56%)	
occurrences (all)	4	3	
Dizziness			
subjects affected / exposed	7 / 84 (8.33%)	5 / 54 (9.26%)	
occurrences (all)	8	5	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	6 / 84 (7.14%)	1 / 54 (1.85%)	
occurrences (all)	6	1	
Anaemia			
subjects affected / exposed	13 / 84 (15.48%)	6 / 54 (11.11%)	
occurrences (all)	19	7	
Eye disorders			
Cataract			

subjects affected / exposed	5 / 84 (5.95%)	0 / 54 (0.00%)	
occurrences (all)	6	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 84 (23.81%)	20 / 54 (37.04%)	
occurrences (all)	33	26	
Abdominal pain			
subjects affected / exposed	6 / 84 (7.14%)	4 / 54 (7.41%)	
occurrences (all)	7	4	
Dry mouth			
subjects affected / exposed	3 / 84 (3.57%)	4 / 54 (7.41%)	
occurrences (all)	3	4	
Constipation			
subjects affected / exposed	5 / 84 (5.95%)	12 / 54 (22.22%)	
occurrences (all)	6	14	
Vomiting			
subjects affected / exposed	6 / 84 (7.14%)	7 / 54 (12.96%)	
occurrences (all)	10	9	
Nausea			
subjects affected / exposed	13 / 84 (15.48%)	6 / 54 (11.11%)	
occurrences (all)	19	9	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 84 (7.14%)	4 / 54 (7.41%)	
occurrences (all)	6	4	
Rash maculo-papular			
subjects affected / exposed	6 / 84 (7.14%)	5 / 54 (9.26%)	
occurrences (all)	7	6	
Dermatitis			
subjects affected / exposed	5 / 84 (5.95%)	0 / 54 (0.00%)	
occurrences (all)	6	0	
Dry skin			
subjects affected / exposed	7 / 84 (8.33%)	5 / 54 (9.26%)	
occurrences (all)	7	6	
Actinic keratosis			

subjects affected / exposed	7 / 84 (8.33%)	3 / 54 (5.56%)	
occurrences (all)	10	3	
Pruritus			
subjects affected / exposed	20 / 84 (23.81%)	8 / 54 (14.81%)	
occurrences (all)	24	13	
Eczema			
subjects affected / exposed	5 / 84 (5.95%)	5 / 54 (9.26%)	
occurrences (all)	5	7	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 84 (3.57%)	4 / 54 (7.41%)	
occurrences (all)	3	5	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 84 (2.38%)	5 / 54 (9.26%)	
occurrences (all)	2	7	
Hypothyroidism			
subjects affected / exposed	8 / 84 (9.52%)	4 / 54 (7.41%)	
occurrences (all)	9	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	16 / 84 (19.05%)	9 / 54 (16.67%)	
occurrences (all)	24	10	
Neck pain			
subjects affected / exposed	2 / 84 (2.38%)	4 / 54 (7.41%)	
occurrences (all)	4	4	
Back pain			
subjects affected / exposed	5 / 84 (5.95%)	5 / 54 (9.26%)	
occurrences (all)	6	5	
Myalgia			
subjects affected / exposed	3 / 84 (3.57%)	5 / 54 (9.26%)	
occurrences (all)	3	6	
Pain in extremity			
subjects affected / exposed	4 / 84 (4.76%)	5 / 54 (9.26%)	
occurrences (all)	5	9	
Muscle spasms			

subjects affected / exposed	5 / 84 (5.95%)	3 / 54 (5.56%)	
occurrences (all)	5	3	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	5 / 84 (5.95%)	0 / 54 (0.00%)	
occurrences (all)	5	0	
Urinary tract infection			
subjects affected / exposed	10 / 84 (11.90%)	4 / 54 (7.41%)	
occurrences (all)	11	5	
Bronchitis			
subjects affected / exposed	6 / 84 (7.14%)	0 / 54 (0.00%)	
occurrences (all)	7	0	
Upper respiratory tract infection			
subjects affected / exposed	6 / 84 (7.14%)	3 / 54 (5.56%)	
occurrences (all)	6	3	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 84 (2.38%)	6 / 54 (11.11%)	
occurrences (all)	2	8	
Hypokalaemia			
subjects affected / exposed	4 / 84 (4.76%)	4 / 54 (7.41%)	
occurrences (all)	6	4	
Hypoalbuminaemia			
subjects affected / exposed	6 / 84 (7.14%)	1 / 54 (1.85%)	
occurrences (all)	12	2	
Decreased appetite			
subjects affected / exposed	14 / 84 (16.67%)	6 / 54 (11.11%)	
occurrences (all)	18	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2016	The purposes of this amendment were to: Note regional laboratory testing for bicarbonate, Add a window for the duration of the REGN2810 infusion, Update the contraception language in the exclusion criteria
23 March 2017	The purpose of the amendment was to revise the protocol based on regulatory agency advice and the internal program review by the sponsor.
03 July 2017	Modified exclusion criteria; Additional safety guidance language added; Added an adverse event of special interest (AESI) to the list of AESIs
29 July 2019	Clarified the details of data cut for the primary analysis for Group 2; Added an interim analysis for Group 1; Clarified eligibility for retreatment; Posttreatment follow-up was extended; Neutralizing antibody analysis was included; Revised exclusion criteria; Modifications for consistency and clarity, and administrative updates

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported