Clinical trial results:
A Phase 2, multicenter, open-label, multi-cohort study to assess safety and efficacy of CC-90011
in combination with nivolumabin subjects with advanced cancers

Summary

EudraCT number	2019-004194-95
Trial protocol	FR GB ES PL IT
Global end of trial date	19 December 2023

Results information

Result version number	v1
This version publication date	26 December 2024
First version publication date	26 December 2024

Trial information

Trial identification

Sponsor protocol code	CC-90011-ST-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04350463
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium,
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@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	31 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to assess the safety and efficacy of CC-90011 in combination with nivolumab in subjects with small cell lung cancer or squamous non-small cell lung cancer who have progressed after 1or 2 lines of therapy.

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	12 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 46
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	92
EEA total number of subjects	76

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)	51
From 65 to 84 years	40
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled in 6 countries.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A 40 mg

Arm description:

Participants with small cell lung cancer (SCLC) and immune checkpoint inhibitor (ICI) naive received capsule of 40 milligram (mg) of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

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

Dosage and administration details:

Nivolumab was administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60 minute infusion

Investigational medicinal product name	CC-90011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

40 mg capsule administered orally

Arm title	Cohort A 60mg

Arm description:

Participants with SCLC and ICI naive received capsule of 60 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

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

Dosage and administration details:

Nivolumab was administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60 minute infusion

Investigational medicinal product name	CC-90011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

40 mg capsule administered orally

Arm title	Cohort B 40 mg

Arm description:

Participants with SCLC and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

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

Dosage and administration details:

Nivolumab was administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60 minute infusion

Investigational medicinal product name	CC-90011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

40 mg capsule administered orally

Arm title	Cohort C

Arm description:

Participants with squamous non-small cell lung cancer (sqNSCLC) and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

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

Dosage and administration details:

Nivolumab was administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60 minute infusion

Investigational medicinal product name	CC-90011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

40 mg capsule administered orally

Number of subjects in period 1	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg
Started	39	2	14
Completed	8	0	0
Not completed	31	2	14
Adverse event, serious fatal	27	2	13
Consent withdrawn by subject	4	-	1
Adverse event, non-fatal	-	-	-
Other reason	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Cohort C
Started	37
Completed	2
Not completed	35
Adverse event, serious fatal	26
Consent withdrawn by subject	4
Adverse event, non-fatal	2
Other reason	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A 40 mg
Reporting group description:	
Participants with small cell lung cancer (SCLC) and immune checkpoint inhibitor (ICI) naive received capsule of 40 milligram (mg) of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.	
Reporting group title	Cohort A 60mg
Reporting group description:	
Participants with SCLC and ICI naive received capsule of 60 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.	
Reporting group title	Cohort B 40 mg
Reporting group description:	
Participants with SCLC and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.	
Reporting group title	Cohort C
Reporting group description:	
Participants with squamous non-small cell lung cancer (sqNSCLC) and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.	

Reporting group values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg
Number of subjects	39	2	14
Age Categorical Units: participants			
< 65 years	21	2	11
>= 65 - < 75 years	16	0	3
>= 75 years	2	0	0
Sex: Female, Male Units: participants			
Female	11	0	5
Male	28	2	9
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	33	2	9
More than one race	0	0	0
Unknown or Not Reported	6	0	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	2
Not Hispanic or Latino	30	2	7
Unknown or Not Reported	7	0	5

Reporting group values	Cohort C	Total	
Number of subjects	37	92	
Age Categorical Units: participants			
< 65 years	17	51	
>= 65 - < 75 years	15	34	
>= 75 years	5	7	
Sex: Female, Male Units: participants			
Female	2	18	
Male	35	74	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	28	72	
More than one race	0	0	
Unknown or Not Reported	9	20	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	7	
Not Hispanic or Latino	23	62	
Unknown or Not Reported	11	23	

End points

End points reporting groups

Reporting group title	Cohort A 40 mg

Reporting group description:

Participants with small cell lung cancer (SCLC) and immune checkpoint inhibitor (ICI) naive received capsule of 40 milligram (mg) of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Reporting group title	Cohort A 60mg

Reporting group description:

Participants with SCLC and ICI naive received capsule of 60 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Reporting group title	Cohort B 40 mg

Reporting group description:

Participants with SCLC and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Reporting group title	Cohort C

Reporting group description:

Participants with squamous non-small cell lung cancer (sqNSCLC) and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Primary: Overall Response Rate

End point title	Overall Response Rate[1]

End point description:

Overall response rate was defined as the percentage of participants in the treated population who had confirmed complete response (CR) or confirmed partial response (PR) as assessed by Investigator review per RECIST v1.1. CR was defined as disappearance of all target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 millimeter (mm). PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Primary

End point timeframe:

Every 6 weeks post Cycle 1 (each cycle is of 28 days) Day 1 for the first 24 weeks and then every 8 weeks until disease progression, new anticancer therapy, death or withdrawal by participants (up to approximately 33 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: Comparison was not planned as per study design.

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: percentage of participants				
number (confidence interval 95%)	10.3 (2.9 to 24.2)	0 (0.0 to 84.2)	0 (0.0 to 23.2)	8.6 (1.8 to 23.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events by Maximal National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE)

End point title	Number of Participants with Adverse Events by Maximal National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE)

End point description:

An Adverse Event (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. AEs were graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (Grade 1=mild, Grade 2=Grade 3 =Prolonged, Grade 4 = Life-threatening, Grade 5 = Death). Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

From the start of study drug through 28 days after the last dose of CC-90011 or until 100 days after last dose of Nivolumab (up to 849 days)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants				
Grade 1	0	0	2	1
Grade 2	14	0	2	4
Grade 3	7	0	3	20
Grade 4	8	2	2	3
Grade 5	10	0	5	6
Missing	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Results with CTCAE Toxicity Grade >=3 for Hematology Parameters

End point title	Number of Participants with Laboratory Results with CTCAE Toxicity Grade >=3 for Hematology Parameters

End point description:

Laboratory results were graded using the Common Terminology Criteria for Adverse Events (CTCAE)

version 5.0 (Grade 3 =Severe, Grade 4 = Life-threatening). Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Cycle 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14 and 18 (each cycle is of 28 days)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants				
Cycle 1 Hemoglobin	3	0	1	3
Cycle 1 Leukocytes	1	0	0	0
Cycle 1 Lymphocytes	5	0	3	3
Cycle 1 Neutrophils	1	1	0	0
Cycle 1 Platelets	3	2	1	0
Cycle 2 Hemoglobin	1	0	0	1
Cycle 2 Lymphocytes	3	0	0	2
Cycle 2 Platelets	5	0	0	1
Cycle 3 Lymphocytes	1	0	1	3
Cycle 3 Platelets	1	0	0	0
Cycle 4 Lymphocytes	1	0	0	1
Cycle 5 Hemoglobin	1	0	0	0
Cycle 5 Lymphocytes	2	0	0	1
Cycle 6 Lymphocytes	1	0	0	1
Cycle 6 Platelets	1	0	0	0
Cycle 7 Lymphocytes	0	0	0	1
Cycle 8 Lymphocytes	0	0	0	1
Cycle 8 Platelets	1	0	0	0
Cycle 9 Lymphocytes	0	0	0	1
Cycle 9 Platelets	1	0	0	0
Cycle 10 Lymphocytes	0	0	0	1
Cycle 10 Platelets	1	0	0	0
Cycle 11 Lymphocytes	0	0	0	1
Cycle 12 Hemoglobin	1	0	0	0
Cycle 14 Platelets	1	0	0	0
Cycle 18 Neutrophils	0	0	0	1
Cycle 18 Platelets	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Results with CTCAE Toxicity Grade >=3 for Chemistry Parameters

End point title	Number of Participants with Laboratory Results with CTCAE Toxicity Grade >=3 for Chemistry Parameters

End point description:

Laboratory results were graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (Grade 3 =Severe, Grade 4 = Life-threatening). Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Cycle 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14 and 18 (Each cycle is of 28 days)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants				
Cycle 1 Alanine Aminotransferase	0	0	2	0
Cycle 1 Albumin	0	0	0	1
Cycle 1 Alkaline Phosphatase	0	0	0	1
Cycle 1 Aspartate Aminotransferase	0	0	1	1
Cycle 1 Bilirubin	1	0	0	1
Cycle 1 Direct Bilirubin	1	0	2	1
Cycle 1 Sodium	3	1	1	1
Cycle 2 Alanine Aminotransferase	1	0	1	0
Cycle 2 Alkaline Phosphatase	0	0	1	0
Cycle 2 Aspartate Aminotransferase	1	0	1	0
Cycle 2 Direct Bilirubin	1	0	1	0
Cycle 2 Glucose	0	0	0	1
Cycle 2 Sodium	1	1	0	1
Cycle 3 Calcium	0	0	0	1
Cycle 3 Direct Bilirubin	0	0	1	0
Cycle 3 Glucose	0	0	0	1
Cycle 3 Potassium	0	0	1	0
Cycle 4 Direct Bilirubin	0	0	1	0
Cycle 4 Sodium	1	0	0	0
Cycle 5 Direct Bilirubin	0	0	1	0
Cycle 6 Calcium	1	0	0	0
Cycle 6 Direct Bilirubin	0	0	1	0
Cycle 6 Sodium	0	0	0	1
Cycle 7 Direct Bilirubin	0	0	1	0
Cycle 8 Direct Bilirubin	0	0	1	0
Cycle 9 Direct Bilirubin	0	0	1	0
Cycle 9 Glucose	0	0	0	1
Cycle 10 Direct Bilirubin	0	0	1	0
Cycle 11 Direct Bilirubin	0	0	1	0
Cycle 14 Direct Bilirubin	1	0	0	0
Cycle 14 Sodium	1	0	0	0
Cycle 16 Potassium	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants receiving Concomitant Medication

End point title	Number of Participants receiving Concomitant Medication

End point description:

Concomitant medication is defined as medications that were either initiated before the first dose of study drug and continued during the study treatment, or initiated on/after the date of the first dose of study drug and on/before the date of treatment discontinuation. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab

End point type	Secondary

End point timeframe:

From first dose till treatment discontinuation due to any reason (Up to approximately 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants	39	2	14	35

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at end of treatment in Vital Sign - Weight

End point title	Change from Baseline at end of treatment in Vital Sign - Weight

End point description:

Baseline value was defined as the last non-missing value on or before the day that first dose of study drug is administered; if multiple values are present for the same date, the average of these values will be used as the baseline. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	1[2]	10	21
Units: kilogram				
arithmetic mean (standard deviation)	-1.88 (± 5.583)	-1.00 (± 99999)	-2.58 (± 5.651)	-4.20 (± 8.065)

Notes:

[2] - 99999 stands for Not Applicable

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at end of treatment in Vital Sign - Diastolic Blood Pressure (DBP) and Systolic Blood Pressure (SBP)

End point title	Change from Baseline at end of treatment in Vital Sign - Diastolic Blood Pressure (DBP) and Systolic Blood Pressure (SBP)

End point description:

Baseline value was defined as the last non-missing value on or before the day that first dose of study drug is administered; if multiple values are present for the same date, the average of these values will be used as the baseline. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	1[3]	11	24
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Systolic Blood Pressure	-8.5 (± 18.35)	5.0 (± 99999)	4.8 (± 14.82)	-11.2 (± 15.19)
Diastolic Blood Pressure	-4.9 (± 10.84)	9.0 (± 99999)	-3.2 (± 6.60)	-3.1 (± 9.89)

Notes:

[3] - 99999 stands for Not Applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at end of treatment in Vital Sign - Temperature

End point title	Change from Baseline at end of treatment in Vital Sign - Temperature

End point description:

Baseline value was defined as the last non-missing value on or before the day that first dose of study drug is administered; if multiple values are present for the same date, the average of these values will be used as the baseline. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	1[4]	11	23
Units: Celsius				
arithmetic mean (standard deviation)	0.01 (± 0.376)	0.20 (± 99999)	0.03 (± 0.388)	-0.04 (± 0.509)

Notes:

[4] - 99999 stands for Not Applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at end of treatment in Vital Sign - Pulse Rate

End point title	Change from Baseline at end of treatment in Vital Sign - Pulse Rate

End point description:

Baseline value was defined as the last non-missing value on or before the day that first dose of study drug is administered; if multiple values are present for the same date, the average of these values will be used as the baseline. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	1[5]	10	24
Units: beats per minute				
arithmetic mean (standard deviation)	-1.0 (± 12.37)	-8.0 (± 99999)	12.0 (± 14.73)	0.4 (± 16.58)

Notes:

[5] - 99999 stands for Not Applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Post-Baseline Grade Shift in Eastern Cooperative Oncology Group Performance (ECOG) Status

End point title	Number of Participants with Post-Baseline Grade Shift in Eastern Cooperative Oncology Group Performance (ECOG) Status

End point description:

ECOG Scale was used to assess performance status. Grades: 0: Fully active, able to carry on all pre-disease performance without restriction. 1: Restricted in physically strenuous activity but ambulatory, able to carry out work of light nature. 2: Ambulatory, capable of self-care, unable to carry out work activities. Up and about more than 50% waking hours. 3: Capable of limited self-care, confined to bed/chair more than 50% waking hours. 4: Completely disabled. Cannot carry on any self-care. Totally confined to bed/chair. 5: Dead. Baseline value was defined as the last non-missing value on or before the day that first dose of study drug is administered; if multiple values are present for the same date, the average of these values will be used as the baseline. Treated population consist of all participants

who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Baseline and up to End of Treatment (107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	1	11	23
Units: participants				
Grade 0 to Grade 0	2	0	4	1
Grade 0 to Grade 1	6	0	1	3
Grade 0 to Grade 2	1	0	0	2
Grade 0 to Grade 3	0	0	0	1
Grade 0 to Grade 4	0	0	0	0
Grade 0 to Grade 5	0	0	0	0
Grade 1 to Grade 0	0	0	0	0
Grade 1 to Grade 1	17	1	5	8
Grade 1 to Grade 2	7	0	0	5
Grade 1 to Grade 3	0	0	1	3
Grade 1 to Grade 4	0	0	0	0
Grade 1 to Grade 5	0	0	0	0
Grade 2 to Grade 0	0	0	0	0
Grade 2 to Grade 1	0	0	0	0
Grade 2 to Grade 2	0	0	0	0
Grade 2 to Grade 3	0	0	0	0
Grade 2 to Grade 4	0	0	0	0
Grade 2 to Grade 5	0	0	0	0
Grade 3 to Grade 0	0	0	0	0
Grade 3 to Grade 1	0	0	0	0
Grade 3 to Grade 2	0	0	0	0
Grade 3 to Grade 3	0	0	0	0
Grade 3 to Grade 4	0	0	0	0
Grade 3 to Grade 5	0	0	0	0
Grade 4 to Grade 0	0	0	0	0
Grade 4 to Grade 1	0	0	0	0
Grade 4 to Grade 2	0	0	0	0
Grade 4 to Grade 3	0	0	0	0
Grade 4 to Grade 4	0	0	0	0
Grade 4 to Grade 5	0	0	0	0
Grade 5 to Grade 0	0	0	0	0
Grade 5 to Grade 1	0	0	0	0
Grade 5 to Grade 2	0	0	0	0
Grade 5 to Grade 3	0	0	0	0
Grade 5 to Grade 4	0	0	0	0
Grade 5 to Grade 5	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events Leading to Dose Reduction of CC-90011

End point title	Number of Participants with Treatment-emergent Adverse Events Leading to Dose Reduction of CC-90011

End point description:

Adverse Event (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. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

From first dose till treatment discontinuation due to any reason (Up to approximately 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants	7	2	3	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events Leading to Dose Interruption of CC-90011

End point title	Number of Participants with Treatment-emergent Adverse Events Leading to Dose Interruption of CC-90011

End point description:

Adverse Event (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. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

From first dose till treatment discontinuation due to any reason (Up to approximately 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants	27	1	6	26

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events Leading to Dose Interruption of Nivolumab

End point title	Number of Participants with Treatment-emergent Adverse Events Leading to Dose Interruption of Nivolumab

End point description:

Adverse Event (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. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

From first dose till treatment discontinuation due to any reason (Up to approximately 107 weeks)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: participants	16	0	3	14

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Progression-Free Survival is the time from first dose of study treatment to the date of the first objectively documented tumor progression as assessed by Investigator review per RECIST v1.1 or death from any cause, whichever occurs first. Disease progression (PD) is defined as an additional 10% increase in tumor burden with a minimum 5 mm absolute increase from time of initial PD. This includes an increase in the sum of diameters of all target lesions and/or the diameters of new measurable lesions compared to the time of the initial PD. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

Every 6 weeks post cycle 1 day 1 (each cycle is of 28 days) for the first 24 weeks and then every 8 weeks until disease progression, new anticancer therapy, death or withdrawal by participant (up to approximately 33 months))

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: days				
arithmetic mean (standard deviation)	126.4 (± 190.29)	33.5 (± 7.78)	65.6 (± 57.23)	184.9 (± 202.20)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Duration of Response was defined as the time from the first occurrence of a confirmed documented response to the time of the first documented tumor progression, as determined by Investigator review per RECIST v1.1, or death from any cause, whichever comes first. CR was defined as disappearance of all target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 millimeter (mm). PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab. Treated Population with confirmed Best Response of CR or PR were included in analysis.

End point type	Secondary

End point timeframe:

Every 6 weeks post cycle 1 day 1 (each cycle is of 28 days) for the first 24 weeks and then every 8 weeks until disease progression, new anticancer therapy, death or withdrawal by participant (up to approximately 33 months))

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	0[6]	0[7]	3
Units: days				
arithmetic mean (standard deviation)	645.0 (± 387.05)	()	()	326.0 (± 201.14)

Notes:

[6] - Only responders are included in analysis

[7] - Only responders are included in analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response

End point title	Time to response

End point description:

Time to response was defined as the time from the first dose of the study drug to the date of the first confirmed documented response (CR or PR), as assessed by Investigator review per RECIST v1.1. CR was defined as disappearance of all target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 millimeter (mm). PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab. Treated Population with confirmed best response of CR or PR.

End point type	Secondary

End point timeframe:

Every 6 weeks post cycle 1 day 1 (each cycle is of 28 days) for the first 24 weeks and then every 8 weeks until disease progression, new anticancer therapy, death or withdrawal by participant (up to approximately 33 months))

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	0[8]	0[9]	3
Units: days				
median (full range (min-max))	82.0 (38 to 91)	(to)	(to)	79.0 (38 to 126)

Notes:

[8] - Only responders are included in analysis.

[9] - Only responders are included in analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Subsequent Therapy

End point title	Time to First Subsequent Therapy

End point description:

Time to First Subsequent Therapy was defined as the time from the first dose of the study drug to the date of the next cancer therapy or death. Treated population consist of all participants who enrolled and took at least one dose of either CC-90011 or nivolumab.

End point type	Secondary

End point timeframe:

From the first dose of study drug to the date of next cancer therapy or death due to any cause (up to approximately 33 months)

End point values	Cohort A 40 mg	Cohort A 60mg	Cohort B 40 mg	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	2	14	35
Units: days				
arithmetic mean (standard deviation)	181.3 (± 183.87)	60.0 (± 2.83)	113.3 (± 111.51)	224.1 (± 203.26)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality was collected from randomization till death due to any cause (Up to approximately 849 days). Serious and Non-Serious Adverse Events were collected from first dose till 100 days after the last dose (up to approximately 849 days).

Adverse event reporting additional description:

All cause mortality was collected for all the enrolled participants. Serious and Non-Serious Adverse Events were collected for all the treated participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Cohort A 40mg

Reporting group description:

Participants with small cell lung cancer (SCLC) and immune checkpoint inhibitor (ICI) naive received capsule of 40 milligram (mg) of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Reporting group title	Cohort A 60mg

Reporting group description:

Participants with SCLC and ICI naive received capsule of 60 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Reporting group title	Cohort B 40 mg

Reporting group description:

Participants with SCLC and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Reporting group title	Cohort C

Reporting group description:

Participants with squamous non-small cell lung cancer (sqNSCLC) and ICI progressor received capsule of 40 mg of CC-90011 orally once in a week in a continuous 28-day cycle. Nivolumab were administered intravenously at a dose of 480 mg every 4 weeks as a 30 minute or a 60-minute intravenous infusion.

Serious adverse events	Cohort A 40mg	Cohort A 60mg	Cohort B 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 39 (51.28%)	2 / 2 (100.00%)	8 / 14 (57.14%)
number of deaths (all causes)	29	2	13
number of deaths resulting from adverse events	10	0	5
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Superior vena cava syndrome			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena cava thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	5 / 39 (12.82%)	0 / 2 (0.00%)	4 / 14 (28.57%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 3
Pyrexia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			

subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
General physical condition abnormal			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cervical cord compression			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	3 / 39 (7.69%)	2 / 2 (100.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	3 / 3	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			

subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Immune-mediated nephritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 39 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Empyema			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Respiratory tract infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort C		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 35 (71.43%)		
number of deaths (all causes)	32		
number of deaths resulting from adverse events	6		
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vena cava thrombosis			

subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	3 / 35 (8.57%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Pyrexia				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	3 / 35 (8.57%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			

Haemoptysis				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pleural effusion				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Bipolar disorder				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
General physical condition abnormal				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Aspartate aminotransferase increased				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Post procedural haemorrhage				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac tamponade				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cervical cord compression				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Neutropenia				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anaemia				

subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemolytic anaemia				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Immune-mediated nephritis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Muscular weakness			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Empyema			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Respiratory tract infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hypokalaemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort A 40mg	Cohort A 60mg	Cohort B 40 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 39 (100.00%)	2 / 2 (100.00%)	14 / 14 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	2
Hypotension			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Superior vena cava syndrome			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Device related thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

Chest discomfort			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	9 / 39 (23.08%)	0 / 2 (0.00%)	5 / 14 (35.71%)
occurrences (all)	10	0	6
Fatigue			
subjects affected / exposed	16 / 39 (41.03%)	1 / 2 (50.00%)	1 / 14 (7.14%)
occurrences (all)	19	1	1
Unevaluable event			
subjects affected / exposed	0 / 39 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Swelling			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	4 / 14 (28.57%)
occurrences (all)	1	0	4
Oedema peripheral			
subjects affected / exposed	4 / 39 (10.26%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	4	0	1
Mucosal inflammation			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Generalised oedema			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Respiratory failure			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nasal ulcer			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Atelectasis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	2	0	4
Dyspnoea			
subjects affected / exposed	6 / 39 (15.38%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	9	0	3
Epistaxis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Hallucination			

subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Blood phosphorus decreased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	2	0	2
Blood creatinine increased			
subjects affected / exposed	7 / 39 (17.95%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	10	0	1
Blood cholesterol increased			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	10	0	0
Blood bilirubin increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 39 (23.08%)	1 / 2 (50.00%)	2 / 14 (14.29%)
occurrences (all)	11	1	2
Alanine aminotransferase increased			
subjects affected / exposed	7 / 39 (17.95%)	1 / 2 (50.00%)	2 / 14 (14.29%)
occurrences (all)	7	1	4
Gamma-glutamyltransferase increased			

subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Headache			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	2	0	2
Neuropathy peripheral			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Somnolence			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Lymphopenia			
subjects affected / exposed	5 / 39 (12.82%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	6	0	0
Neutropenia			
subjects affected / exposed	10 / 39 (25.64%)	1 / 2 (50.00%)	2 / 14 (14.29%)
occurrences (all)	22	1	2
Thrombocytopenia			
subjects affected / exposed	25 / 39 (64.10%)	1 / 2 (50.00%)	5 / 14 (35.71%)
occurrences (all)	60	2	7
Anaemia			
subjects affected / exposed	21 / 39 (53.85%)	1 / 2 (50.00%)	8 / 14 (57.14%)
occurrences (all)	37	1	9
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	4	0	2
Haematochezia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Dysphagia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Dry mouth			

subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	8 / 39 (20.51%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	13	0	0
Constipation			
subjects affected / exposed	6 / 39 (15.38%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	6	0	3
Abdominal pain upper			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Abdominal pain			
subjects affected / exposed	6 / 39 (15.38%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	6	0	1
Oesophagitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	2	0	2
Stomatitis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Hepatic cytolysis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dry skin			

subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Dermatitis acneiform			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Rash papular			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	5 / 39 (12.82%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	6	0	1
Pruritus			
subjects affected / exposed	5 / 39 (12.82%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	8	0	0
Petechiae			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	6 / 39 (15.38%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	6	0	0
Hyperthyroidism			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			

Arthritis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 39 (2.56%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	4 / 39 (10.26%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	4	1	0
Sacral pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	8 / 39 (20.51%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	9	0	2
Infections and infestations			
Folliculitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Implant site infection			

subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	2
Respiratory tract infection			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Tooth abscess			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 39 (30.77%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	14	0	3
Hypercholesterolaemia			
subjects affected / exposed	4 / 39 (10.26%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	5	0	0
Hyperglycaemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	6	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	4	0	0
Hypoalbuminaemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	4	0	1
Hypocalcaemia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	2

Hypochloraemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	3	0	3
Hypomagnesaemia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Hyponatraemia			
subjects affected / exposed	4 / 39 (10.26%)	1 / 2 (50.00%)	4 / 14 (28.57%)
occurrences (all)	11	2	6
Hypophosphataemia			
subjects affected / exposed	3 / 39 (7.69%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	1

Non-serious adverse events	Cohort C		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 35 (94.29%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Superior vena cava syndrome			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Device related thrombosis			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	12 / 35 (34.29%)		
occurrences (all)	14		
Fatigue			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Unevaluable event			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Swelling			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	9 / 35 (25.71%)		
occurrences (all)	9		
Oedema peripheral			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Generalised oedema			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Immune system disorders			

Contrast media reaction subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Respiratory failure subjects affected / exposed occurrences (all) Nasal ulcer subjects affected / exposed occurrences (all) Atelectasis subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Haemoptysis subjects affected / exposed occurrences (all) Hypoxia subjects affected / exposed occurrences (all)	 2 / 35 (5.71%) 2 0 / 35 (0.00%) 0 2 / 35 (5.71%) 2 9 / 35 (25.71%) 11 9 / 35 (25.71%) 11 3 / 35 (8.57%) 4 4 / 35 (11.43%) 7 0 / 35 (0.00%) 0		
Psychiatric disorders Anxiety disorder subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all) Insomnia	 0 / 35 (0.00%) 0 0 / 35 (0.00%) 0		

subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Hallucination			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Investigations			
C-reactive protein increased			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Blood potassium decreased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Blood phosphorus decreased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	4		
Blood creatinine increased			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Blood cholesterol increased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Alanine aminotransferase increased			

subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Sinus tachycardia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	6		
Neuropathy peripheral			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Somnolence			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	7		
Neutropenia			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Thrombocytopenia			
subjects affected / exposed	13 / 35 (37.14%)		
occurrences (all)	32		
Anaemia			
subjects affected / exposed	16 / 35 (45.71%)		
occurrences (all)	22		
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Haematochezia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Dyspepsia			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	6		
Abdominal pain upper			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Oesophagitis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hepatic cytolysis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Ecchymosis			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Dermatitis acneiform			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Alopecia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Petechiae			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Renal failure			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Hyperthyroidism			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Bone pain			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	4		
Musculoskeletal pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Neck pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Sacral pain			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	8		
Infections and infestations			

Folliculitis subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Implant site infection subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Pneumonia subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 4		
Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Tooth abscess subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
COVID-19 subjects affected / exposed occurrences (all)	6 / 35 (17.14%) 6		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	10 / 35 (28.57%) 11		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Hypoalbuminaemia			

subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Hypochloraemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	6		
Hypophosphataemia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2020	The primary purpose of this protocol amendment is to address the 2 serious adverse events (SAEs) reported in the first two subjects treated in Study CC-90011-ST-002, and the resulting implementation to reduce the starting dose of CC-90011 to 40 mg. Implementation of this dose reduction was communicated to all participating sites through an administrative letter on 18 Aug 2020. This dose reduction is consistent with Protocol CC-90011-ST-002 language in Section 7.3.2 and the 2 SAEs of Grade 4 thrombocytopenia are consistent with the known safety profile of CC-90011.
02 March 2021	The primary purpose of this protocol amendment is to include a risk benefit assessment and additional language for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/coronavirus-19 (COVID-19), as well as to update nivolumab guidance for male contraception and update adverse event management algorithms based on the nivolumab Investigator's Brochure (IB) version 19 addendum 01 and to extend pharmacokinetics and immunogenicity collection to all cohorts.
30 April 2022	This Protocol Amendment is to reduce the duration of survival follow-up period. As of this amendment, 92 patients have been enrolled across the 3 cohorts, with 41 patientsin Cohort A (4 confirmed responses), 15 patients in Cohort B (0 confirmed responses), and 36 patients in Cohort C (2 confirmed responses).With thelimited number of enrolled patients, overall survival (OS) may not provide meaningful interpretative data. As a result, OS is being moved to an exploratory objective and endpoint. The survival follow-up period is being modifiedby removing the up to 2-year duration and adding in that survival follow-up will stop after the 100-day safety follow-up visit of the last subject on study treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported