



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

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

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|---|-----------------------|--|--|
| 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) | 2 / 35 (5.71%) 2 | | |
| Nasal ulcer subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Atelectasis subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 2 | | |
| Cough subjects affected / exposed occurrences (all) | 9 / 35 (25.71%) 11 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 9 / 35 (25.71%) 11 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 3 / 35 (8.57%) 4 | | |
| Haemoptysis subjects affected / exposed occurrences (all) | 4 / 35 (11.43%) 7 | | |
| Hypoxia subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Psychiatric disorders | | | |
| Anxiety disorder subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Insomnia | | | |

| | | | |
|---------------------------------------|----------------|--|--|
| 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 occurrences (all) | 0 / 35 (0.00%) 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 | 0 / 35 (0.00%) | | |
| occurrences (all) | 0 | | |
| Implant site infection | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | | |
| occurrences (all) | 4 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences (all) | 1 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences (all) | 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 6 / 35 (17.14%) | | |
| occurrences (all) | 6 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 10 / 35 (28.57%) | | |
| occurrences (all) | 11 | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences (all) | 1 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences (all) | 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 patients in Cohort A (4 confirmed responses), 15 patients in Cohort B (0 confirmed responses), and 36 patients in Cohort C (2 confirmed responses). With the limited 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 modified by 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