Clinical trial results:
A Phase 3, Randomized, Open-Label Study to Compare Ociperlimab (BGB-A1217) Plus Tislelizumab (BGB-A317) Versus Durvalumab in Patients With Locally Advanced, Unresectable, PD-L1-Selected Non-Small Cell Lung Cancer Whose Disease Has Not Progressed After Concurrent Chemoradiotherapy

Summary

EudraCT number	2020-004656-14
Trial protocol	FR DE NL PL ES IT
Global end of trial date	17 October 2023

Results information

Result version number	v1 (current)
This version publication date	25 October 2024
First version publication date	25 October 2024

Trial information

Trial identification

Sponsor protocol code	BGB-A317-A1217-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04866017
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BeiGene
Sponsor organisation address	1840 Gateway Drive, San Mateo, CA , United States, 94404
Public contact	BeiGene Clinical Support, BeiGene USA, Inc., 1 877-828-5568, ClinicalTrials@beigene.com
Scientific contact	BeiGene Clinical Support, BeiGene USA, Inc., 1 877-828-5568, ClinicalTrials@beigene.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	17 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and efficacy of ociperlimab in combination with tislelizumab compared to durvalumab in adults with stage III unresectable PD-L1-selected non-small cell lung cancer whose disease has not progressed after cCRT.

Protection of trial subjects:

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of GCP as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki. The IEC/IRB-approved ICF was signed and dated by the subject or the subject's legally authorized representative before his or her participation in the study. A copy of each signed ICF was provided to the subject or the subject's legally authorized representative. All signed and dated ICFs were retained in each patient's study file or in the site file. For any updated or revised ICFs, written informed consent was obtained using the IEC/IRB-approved updated/revised ICFs for continued participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 45
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Spain: 5
Worldwide total number of subjects	63
EEA total number of subjects	5

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)	33
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in multiple study centers in Taiwan, China, Spain , United States, and Australia. The first participant was consented on June 17th, 2021, and the last participant completed on October 17th, 2023. The decision to terminate the study was made on July 11th, 2023.

Pre-assignment

Screening details:

This study began under Protocol Amendment (PA) 1. PA 2 was later introduced, but no participants enrolled under it before the study ended. PA 2 revised eligibility criteria, treatment, objectives, and endpoints, and excluded participants from PA 1 in the primary and secondary efficacy analyses.

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	Ociperlimab + Tislelizumab + cCRT

Arm description:

Participants enrolled in PA 1 received two cycles of ociperlimab (900 mg) and tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). Chemotherapy regimens varied based on investigator discretion, including options such as cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. After the cCRT phase, participants continued ociperlimab and tislelizumab treatment for up to one year.

Arm type	Experimental
Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	
Other name	BGB-A317
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg intravenously every three weeks

Investigational medicinal product name	Ociperlimab
Investigational medicinal product code	
Other name	BGB-A1217
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

900 milligrams (mg) intravenously every three weeks

Arm title	Tislelizumab + cCRT

Arm description:

Participants in PA 1 received two cycles of tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). The chemotherapy regimen was determined by the investigator and included options like cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. Following the cCRT phase, participants continued tislelizumab treatment for up to one year.

Arm type	Experimental
Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	
Other name	BGB-A317
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg intravenously every three weeks

Arm title	cCRT Followed by Durvalumab

Arm description:

Participants in PA 1 received two cycles of concurrent chemoradiotherapy (cCRT), followed by durvalumab (10 mg/kg intravenously every 2 weeks, or 1500 mg every 4 weeks if locally approved). The chemotherapy regimen was chosen by the investigator and included options such as cisplatin with etoposide, carboplatin with paclitaxel, or pemetrexed with a platinum agent for non-squamous histology; alongside radiotherapy. After cCRT, participants continued durvalumab treatment for up to one year.

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

Dosage and administration details:

10 milligrams per kilogram (mg/kg) intravenously once every 2 weeks (or 1500 mg intravenously once every 4 weeks where the dosage has been approved by a local health authority)

Number of subjects in period 1	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab
Started	22	19	22
Treated	22	18	22
Completed	0	0	0
Not completed	22	19	22
Consent withdrawn by subject	1	-	1
Physician decision	-	1	-
Death	8	4	8
Study Terminated by Sponsor	13	14	13

Baseline characteristics

Reporting groups

Reporting group title	Ociperlimab + Tislelizumab + cCRT

Reporting group description:

Participants enrolled in PA 1 received two cycles of ociperlimab (900 mg) and tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). Chemotherapy regimens varied based on investigator discretion, including options such as cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. After the cCRT phase, participants continued ociperlimab and tislelizumab treatment for up to one year.

Reporting group title	Tislelizumab + cCRT

Reporting group description:

Participants in PA 1 received two cycles of tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). The chemotherapy regimen was determined by the investigator and included options like cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. Following the cCRT phase, participants continued tislelizumab treatment for up to one year.

Reporting group title	cCRT Followed by Durvalumab

Reporting group description:

Participants in PA 1 received two cycles of concurrent chemoradiotherapy (cCRT), followed by durvalumab (10 mg/kg intravenously every 2 weeks, or 1500 mg every 4 weeks if locally approved). The chemotherapy regimen was chosen by the investigator and included options such as cisplatin with etoposide, carboplatin with paclitaxel, or pemetrexed with a platinum agent for non-squamous histology; alongside radiotherapy. After cCRT, participants continued durvalumab treatment for up to one year.

Reporting group values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab
Number of subjects	22	19	22
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
The Intent-to-Treat (ITT) Analysis Set is defined as all randomized participants.			
Units: years arithmetic mean standard deviation	 63.4 ± 7.51	 62.4 ± 9.27	 64.1 ± 7.36
Gender categorical			
The Intent-to-Treat (ITT) Analysis Set is defined as all randomized participants.			
Units: Subjects			

Female	3	5	0
Male	19	14	22

Reporting group values	Total		
Number of subjects	63		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
The Intent-to-Treat (ITT) Analysis Set is defined as all randomized participants.			
Units: years arithmetic mean standard deviation	- -		
Gender categorical			
The Intent-to-Treat (ITT) Analysis Set is defined as all randomized participants.			
Units: Subjects			
Female	8		
Male	55		

End points

End points reporting groups

Reporting group title	Ociperlimab + Tislelizumab + cCRT

Reporting group description:

Participants enrolled in PA 1 received two cycles of ociperlimab (900 mg) and tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). Chemotherapy regimens varied based on investigator discretion, including options such as cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. After the cCRT phase, participants continued ociperlimab and tislelizumab treatment for up to one year.

Reporting group title	Tislelizumab + cCRT

Reporting group description:

Participants in PA 1 received two cycles of tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). The chemotherapy regimen was determined by the investigator and included options like cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. Following the cCRT phase, participants continued tislelizumab treatment for up to one year.

Reporting group title	cCRT Followed by Durvalumab

Reporting group description:

Participants in PA 1 received two cycles of concurrent chemoradiotherapy (cCRT), followed by durvalumab (10 mg/kg intravenously every 2 weeks, or 1500 mg every 4 weeks if locally approved). The chemotherapy regimen was chosen by the investigator and included options such as cisplatin with etoposide, carboplatin with paclitaxel, or pemetrexed with a platinum agent for non-squamous histology; alongside radiotherapy. After cCRT, participants continued durvalumab treatment for up to one year.

Primary: Progression-Free Survival (PFS) as Assessed by the Independent Review Committee (IRC)

End point title	Progression-Free Survival (PFS) as Assessed by the Independent Review Committee (IRC)[1]

End point description:

PFS is defined as the time from the date of randomization to the date of first documentation of disease progression as assessed by the IRC per Response Evaluation Criteria in Solid Tumors (RECIST) Version (v) 1.1 or death, whichever occurred first.

The primary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Primary

End point timeframe:

From randomization through to the end of study, planned duration was 20 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: Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[2] - No participants were enrolled under PA 2.

[3] - No participants were enrolled under PA 2.

[4] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Defined as the time from the date of randomization until the date of death due to any cause. This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

From randomization through to the end of study, planned duration was 20 months

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[5] - No participants were enrolled under PA 2.

[6] - No participants were enrolled under PA 2.

[7] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

Defined as the percentage of participants who achieved a complete response (CR) or partial response (PR) assessed by both the IRC and investigators per RECIST v1.1. This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

From randomization through to the end of study, planned duration was 20 months

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[8] - No participants were enrolled under PA 2.

[9] - No participants were enrolled under PA 2.

[10] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Defined as the time from the first determination of a confirmed objective response assessed by both the IRC and investigators per RECIST v1.1 until the first documentation of disease progression or death, whichever occurs first. This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

From randomization through to the end of study, planned duration was 20 months

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[11] - No participants were enrolled under PA 2.

[12] - No participants were enrolled under PA 2.

[13] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Death or Distant Metastasis (TTDM) as Assessed by the Investigator

End point title	Time to Death or Distant Metastasis (TTDM) as Assessed by the Investigator

End point description:

defined as the time from the date of randomization until the first date of distant metastasis assessed by both the IRC and investigators, or death. Distant metastasis is defined as any new lesion that is outside of the radiation field per RECIST v1.1 or proven by biopsy. This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

From randomization through to the end of study, planned duration was 20 months

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[14]	0[15]	0[16]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[14] - No participants were enrolled under PA 2.

[15] - No participants were enrolled under PA 2.

[16] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival 2 (PFS2)

End point title	Progression-Free Survival 2 (PFS2)

End point description:

Defined as the time from randomization to the disease progression after next line of treatment, or death from any cause, whichever occurs first. This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

From randomization through to the end of study, planned duration was 20 months

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[17]	0[18]	0[19]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[17] - No participants were enrolled under PA 2.

[18] - No participants were enrolled under PA 2.

[19] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AEs)

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

End point description:

Number of participants with treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) determined according to National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0). The Safety Analysis Set included all randomized patients who received any dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose to 30 days after the last dose or initiation of a new anticancer therapy, whichever occured first; through study completion data cut-off date of October 17th, 2023 (maximum time on treatment was 16 months)

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	18	22	
Units: Count of Participants				
number (not applicable)				
TEAEs	22	18	22	
SAEs	11	8	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) Global Health Status

End point title	Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) Global Health Status

End point description:

Mean change from baseline in EORTC QLQ-C30 Global Health Status/Quality of Life score. The EORTC QLQ-C30 v3.0 is a questionnaire that assesses quality of life of participants with cancer. It includes global health status and quality of life questions related to overall health in which participants respond based on a 7-point scale, where 1 is very poor and 7 is excellent. Raw scores are transformed into a 0 to 100 scale via linear transformation. A higher score indicates better health outcomes.

This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

Every 2 Cycles (6 weeks) until End of Treatment (each cycle is 21 days)

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[20]	0[21]	0[22]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[20] - No participants were enrolled under PA 2.

[21] - No participants were enrolled under PA 2.

[22] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Related Quality of Life (HRQoL) as Assessed by Quality of Life QuestionnaireLung Cancer 13 (QLQ-LC13)

End point title	Change From Baseline in Health Related Quality of Life (HRQoL) as Assessed by Quality of Life QuestionnaireLung Cancer 13 (QLQ-LC13)

End point description:

Mean change from baseline in QLQ-CL13 scores for coughing, dyspnea, and chest pain. The QLQ-LC13 is a questionnaire that measures lung cancer-specific disease and treatment symptoms. It includes questions about specific symptoms in which participants respond based on a 4-point scale, where 1 is "not at all" and 4 is "very much". Raw scores are transformed into a 0 to 100 scale via linear transformation. A lower score indicates an improvement in symptoms.

This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

Every 2 Cycles (6 weeks) until End of Treatment (each cycle is 21 days)

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[23]	0[24]	0[25]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[23] - No participants were enrolled under PA 2.

[24] - No participants were enrolled under PA 2.

[25] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Related Quality of Life (HRQoL) as Assessed by European Quality of Life-5 Dimensions (EQ-5D-5L)

End point title	Change From Baseline in Health Related Quality of Life (HRQoL) as Assessed by European Quality of Life-5 Dimensions (EQ-5D-5L)

End point description:

The EuroQol 5D-5L a descriptive system that comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. The participant is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension. The digits for the five dimensions can be combined into a 5-digit number that describes the participant's health state.

This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

Every 2 Cycles (6 weeks) until End of Treatment (each cycle is 21 days)

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[26]	0[27]	0[28]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[26] - No participants were enrolled under PA 2.

[27] - No participants were enrolled under PA 2.

[28] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Ociperlimab

End point title	Serum Concentration of Ociperlimab[29]

End point description:

Serum concentrations of ociperlimab were measured for participants in the Ociperlimab + Tislelizumab + cCRT treatment group at predose (within 60 minutes before starting infusion) and postdose (within 30 minutes after the end of infusion). End of Treatment (EOT) visits occurred within 7 days after the date the investigator determined that study treatment would no longer be used, or before the initiation of a new anticancer treatment, whichever occurred first. The Pharmacokinetics (PK) Analysis Set includes all patients who receive any dose of any component of study drugs and for whom any postdose PK data are available.

End point type	Secondary

End point timeframe:

Predose at Day 1 of Cycles 1, 2, 5, 9, and 17; postdose on Day 1 of Cycles 1, 5 and EOT visit (Each Cycle was 21 days)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

End point values	Ociperlimab + Tislelizumab + cCRT			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: ug/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Predose	18 (± 0000)			
Cycle 1 Day 1 Postdose	312 (± 45.82)			
Cycle 2 Day 1 Predose	34.54 (± 63.19)			
Cycle 2 Day 1 Postdose	0 (± 0)			
Cycle 5 Day 1 Predose	74.86 (± 61.76)			
Cycle 5 Day 1 Postdose	339.31 (± 38.21)			
Cycle 9 Day 1 Predose	52.4 (± 82.40)			
Cycle 9 Day 1 Postdose	0 (± 0)			
Cycle 17 Day 1 Predose	81.35 (± 53.83)			
Cycle 17 Day 1 Postdose	0 (± 0)			
End of Treatment	94.94 (± 232.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Tislelizumab for Participants in the Ociperlimab + Tislelizumab + cCRT Treatment Group

End point title	Serum Concentration of Tislelizumab for Participants in the Ociperlimab + Tislelizumab + cCRT Treatment Group[30]

End point description:

Serum concentrations of tislelizumab were collected for participants in the Ociperlimab + Tislelizumab + cCRT treatment group at predose (within 60 minutes before starting infusion) and postdose (within 30 minutes after the end of infusion). End of Treatment (EOT) visits occurred within 7 days after the date investigator determined that study treatment would no longer be used, or before the initiation of a new anticancer treatment, whichever occurred first. The Pharmacokinetics (PK) Analysis Set includes all patients who receive any dose of any component of study drugs and for whom any postdose PK data are available.

End point type	Secondary

End point timeframe:

Predose at Day 1 of Cycles 1, 2, 5, 9, 17; postdose on Day 1 of Cycles 1 and 5, and EOT visit (each cycle was 21 days)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

End point values	Ociperlimab + Tislelizumab + cCRT			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Predose	9999 (± 9999)			
Cycle 1 Day 1 Postdose	72.20 (± 26.27)			
Cycle 2 Day 1 Predose	15.91 (± 78.83)			
Cycle 2 Day 1 Postdose	0 (± 0)			
Cycle 5 Day 1 Predose	34.10 (± 49.67)			
Cycle 5 Day 1 Postdose	97.08 (± 23.09)			
Cycle 9 Day 1 Predose	30.22 (± 55.34)			
Cycle 9 Day 1 Postdose	0 (± 0)			
Cycle 17 Day 1 Predose	32.24 (± 156.53)			
Cycle 17 Day 1 Postdose	0 (± 0)			
End of Treatment	49.55 (± 89.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Tislelizumab for Participants in the Tislelizumab

+ cCRT Treatment Group

End point title	Serum Concentration of Tislelizumab for Participants in the Tislelizumab + cCRT Treatment Group[31]

End point description:

Serum concentrations of tislelizumab were collected for participants in the Tislelizumab + cCRT treatment group at predose (within 60 minutes prior to infusion initiation) and postdose (within 30 minutes after the completion of infusion). End of Treatment (EOT) visits occurred within 7 days after the date investigator determined that study treatment would no longer be used, or before the initiation of a new anticancer treatment, whichever occurred first.
PK Analysis Set; Tislelizumab concentration data are reported here for participants in the Tislelizumab + cCRT treatment group. Only participants with available data are included at each time point.

End point type	Secondary

End point timeframe:

Predose at Day 1 of Cycles 1, 2, 5, 9, and 17; postdose on Day 1 of Cycles 1 and 5, and EOT visit (Each Cycle is 21 days)

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

End point values	Tislelizumab + cCRT			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Predose	0000 (± 0000)			
Cycle 1 Day 1 Postdose	73.41 (± 18.53)			
Cycle 2 Day 1 Predose	19.69 (± 27.01)			
Cycle 2 Day 1 Postdose	0 (± 0)			
Cycle 5 Day 1 Predose	37.64 (± 47.00)			
Cycle 5 Day 1 Postdose	100.26 (± 29.25)			
Cycle 9 Day 1 Predose	36.98 (± 39.63)			
Cycle 9 Day 1 Postdose	0 (± 0)			
Cycle 17 Day 1 Predose	41.29 (± 55.41)			
Cycle 17 Day 1 Postdose	0 (± 0)			
End of Treatment	40.18 (± 139.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenic Responses to Ociperlimab as Assessed by the Detection of Treatment Emergent Anti-Drug Antibodies (ADAs)

End point title	Immunogenic Responses to Ociperlimab as Assessed by the Detection of Treatment Emergent Anti-Drug Antibodies (ADAs)[32]

End point description:

Defined as the sum of treatment-boosted and treatment-induced ADA participants as a proportion percentage of the ADA-evaluable participants population and is synonymous with 'ADA Incidence'. ADA samples were collected for participants randomized to Arm A (ociperlimab and tislelizumab). The Immunogenicity Analysis Set includes all participants who received any dose of any component of study drugs and for whom both baseline antidrug antibody (ADA) and at least 1 postbaseline ADA result were available.

End point type	Secondary

End point timeframe:

Predose (within 60 minutes before dose) on Day 1 of Cycles 1, 2, 5, 9, 17, and the EOT Visit (Each cycle is 21 days). Maximum number of treatment cycles was 19

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

End point values	Ociperlimab + Tislelizumab + cCRT			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Count of Participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenic Responses to Tislelizumab as Assessed by the Detection of Treatment Emergent Anti-Drug Antibodies (ADAs)

End point title	Immunogenic Responses to Tislelizumab as Assessed by the Detection of Treatment Emergent Anti-Drug Antibodies (ADAs)[33]

End point description:

Defined as the sum of treatment-boosted and treatment-induced ADA participants as a proportion percentage of the ADA-evaluable participants population and is synonymous with 'ADA Incidence'. ADA samples were collected for participants randomized to Arm A (Ociperlimab + Tislelizumab + cCRT) and Arm B (Tislelizumab + cCRT). The Immunogenicity Analysis Set includes all participants who received any dose of any component of study drugs and for whom both baseline antidrug antibody (ADA) and at least 1 postbaseline ADA result were available.

End point type	Secondary

End point timeframe:

Predose (within 60 minutes before dose) on Day 1 of Cycles 1, 2, 5, 9, 17, and the EOT Visit (Each cycle is 21 days, maximum number of treatment cycles was 19)

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: Count of Participants				
number (not applicable)	10	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Programmed Death-Ligand 1 (PD-L1) and T-cell Immunoreceptor With Ig and ITIM Domains (TIGIT) Expression in Archival and/or Fresh Tumor Tissues

End point title	Programmed Death-Ligand 1 (PD-L1) and T-cell Immunoreceptor With Ig and ITIM Domains (TIGIT) Expression in Archival and/or Fresh Tumor Tissues

End point description:

This secondary endpoint was specified in PA 2 and excludes participants enrolled under PA 1. No participants were enrolled under PA 2.

End point type	Secondary

End point timeframe:

From randomization through to the end of study, planned duration was 20 months

End point values	Ociperlimab + Tislelizumab + cCRT	Tislelizumab + cCRT	cCRT Followed by Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[34]	0[35]	0[36]	
Units: Count of Participants				
number (not applicable)				

Notes:

[34] - No participants were enrolled under PA 2.

[35] - No participants were enrolled under PA 2.

[36] - No participants were enrolled under PA 2.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to 30 days after the last dose or initiation of a new anticancer therapy, whichever occured first; through study completion data cut-off date of October 17th, 2023 (maximum time on treatment was 16 months)

Adverse event reporting additional description:

All-cause mortality is reported for all randomized participants. Serious and other adverse events include all randomized participants who received ≥ 1 dose of any study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	Ociperlimab + Tislelizumab + cCRT

Reporting group description:

Participants enrolled in PA 1 received two cycles of ociperlimab (900 mg) and tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). Chemotherapy regimens varied based on investigator discretion, including options such as cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. After the cCRT phase, participants continued ociperlimab and tislelizumab treatment for up to one year.

Reporting group title	cCRT Followed by Durvalumab

Reporting group description:

Participants in PA 1 received two cycles of concurrent chemoradiotherapy (cCRT), followed by durvalumab (10 mg/kg intravenously every 2 weeks, or 1500 mg every 4 weeks if locally approved). The chemotherapy regimen was chosen by the investigator and included options such as cisplatin with etoposide, carboplatin with paclitaxel, or pemetrexed with a platinum agent for non-squamous histology; alongside radiotherapy. After cCRT, participants continued durvalumab treatment for up to one year.

Reporting group title	Tislelizumab + cCRT

Reporting group description:

Participants in PA 1 received two cycles of tislelizumab (200 mg) intravenously every three weeks, combined with concurrent chemoradiotherapy (cCRT). The chemotherapy regimen was determined by the investigator and included options like cisplatin with etoposide, carboplatin with paclitaxel, or platinum-based regimens with pemetrexed for non-squamous histology; alongside radiotherapy. Following the cCRT phase, participants continued tislelizumab treatment for up to one year.

Serious adverse events	Ociperlimab + Tislelizumab + cCRT	cCRT Followed by Durvalumab	Tislelizumab + cCRT
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 22 (50.00%)	8 / 22 (36.36%)	8 / 18 (44.44%)
number of deaths (all causes)	8	8	4
number of deaths resulting from adverse events	1	2	1
Investigations			
Neutrophil count decreased			

subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (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
Platelet count decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (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
Transaminases increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (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
White blood cell count decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected neoplasm			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (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
Injury, poisoning and procedural complications			
Radiation oesophagitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation pneumonitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Stomatitis			

subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (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
Respiratory, thoracic and mediastinal disorders			
Bronchopleural fistula			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Interstitial lung disease			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	2 / 18 (11.11%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	3 / 22 (13.64%)	0 / 22 (0.00%)	2 / 18 (11.11%)
occurrences causally related to treatment / all	3 / 3	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pathological fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (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 pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (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
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hyponatraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Ociperlimab + Tislelizumab + cCRT	cCRT Followed by Durvalumab	Tislelizumab + cCRT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)	22 / 22 (100.00%)	18 / 18 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Cancer pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Hypertension			
subjects affected / exposed	3 / 22 (13.64%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences (all)	3	2	2
Haematoma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Aortic arteriosclerosis			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Venous thrombosis limb			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 22 (18.18%)	5 / 22 (22.73%)	1 / 18 (5.56%)
occurrences (all)	4	5	1
Chest discomfort			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
Facial pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Chills			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Chest pain			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	3	2	1
Oedema peripheral			
subjects affected / exposed	1 / 22 (4.55%)	3 / 22 (13.64%)	0 / 18 (0.00%)
occurrences (all)	1	4	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			

subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	4	0	0
Fatigue			
subjects affected / exposed	4 / 22 (18.18%)	2 / 22 (9.09%)	4 / 18 (22.22%)
occurrences (all)	5	2	5
Puncture site pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	3 / 22 (13.64%)	0 / 22 (0.00%)	4 / 18 (22.22%)
occurrences (all)	5	0	7
Swelling face			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Drug hypersensitivity			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Hypersensitivity			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Infusion related hypersensitivity reaction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Atelectasis			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	4 / 22 (18.18%)	5 / 22 (22.73%)	5 / 18 (27.78%)
occurrences (all)	5	6	6
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	4 / 22 (18.18%)	2 / 22 (9.09%)	2 / 18 (11.11%)
occurrences (all)	4	2	2
Dysphonia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Haemoptysis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	3 / 18 (16.67%)
occurrences (all)	2	4	3
Hiccups			
subjects affected / exposed	3 / 22 (13.64%)	3 / 22 (13.64%)	2 / 18 (11.11%)
occurrences (all)	4	4	4
Hydrothorax			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Immune-mediated lung disease			
subjects affected / exposed	3 / 22 (13.64%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Interstitial lung disease			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	3 / 22 (13.64%)	3 / 22 (13.64%)	2 / 18 (11.11%)
occurrences (all)	3	3	2

Pleural effusion			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Pleural thickening			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences (all)	2	2	2
Rhinorrhoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Pulmonary oedema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	2 / 18 (11.11%)
occurrences (all)	0	2	3
Psychiatric disorders			
Tic			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	3 / 22 (13.64%)	1 / 22 (4.55%)	3 / 18 (16.67%)
occurrences (all)	4	1	3
Depression			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	2 / 18 (11.11%)
occurrences (all)	3	1	3
Bilirubin conjugated increased			

subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 22 (27.27%)	4 / 22 (18.18%)	0 / 18 (0.00%)
occurrences (all)	10	5	0
Blood bilirubin unconjugated increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	8 / 22 (36.36%)	6 / 22 (27.27%)	0 / 18 (0.00%)
occurrences (all)	15	9	0
Amylase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Blood chloride decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	4
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	2	1	4
Blood fibrinogen increased			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences (all)	4	3	2
Blood creatinine decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	2	3	2
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Blood urea increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	2 / 18 (11.11%)
occurrences (all)	3	0	4
Ejection fraction decreased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	3 / 18 (16.67%)
occurrences (all)	4	2	7
Fibrin D dimer increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	2	2
Lymphocyte count decreased			
subjects affected / exposed	5 / 22 (22.73%)	6 / 22 (27.27%)	5 / 18 (27.78%)
occurrences (all)	7	10	5
Neutrophil count decreased			
subjects affected / exposed	14 / 22 (63.64%)	13 / 22 (59.09%)	5 / 18 (27.78%)
occurrences (all)	31	29	13
Myoglobin blood increased			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Neutrophil count increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	8 / 22 (36.36%)	10 / 22 (45.45%)	5 / 18 (27.78%)
occurrences (all)	12	16	6
Occult blood positive			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	3 / 22 (13.64%)	3 / 22 (13.64%)	1 / 18 (5.56%)
occurrences (all)	6	3	1
Weight decreased			
subjects affected / exposed	4 / 22 (18.18%)	4 / 22 (18.18%)	2 / 18 (11.11%)
occurrences (all)	4	4	2
Troponin T increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 22 (4.55%)	4 / 22 (18.18%)	2 / 18 (11.11%)
occurrences (all)	1	4	2
Red blood cell count decreased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
White blood cell count increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			

subjects affected / exposed	15 / 22 (68.18%)	13 / 22 (59.09%)	10 / 18 (55.56%)
occurrences (all)	45	41	25
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	3	1
Radiation fibrosis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Radiation pneumonitis			
subjects affected / exposed	0 / 22 (0.00%)	5 / 22 (22.73%)	2 / 18 (11.11%)
occurrences (all)	0	7	2
Radiation oesophagitis			
subjects affected / exposed	6 / 22 (27.27%)	9 / 22 (40.91%)	3 / 18 (16.67%)
occurrences (all)	6	10	3
Skin abrasion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Radiation skin injury			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	5 / 18 (27.78%)
occurrences (all)	2	1	5
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			

subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Bundle branch block right			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	2
Sinus bradycardia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Pericardial effusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Ventricular arrhythmia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Supraventricular extrasystoles			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Ventricular extrasystoles			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	2 / 22 (9.09%)	3 / 22 (13.64%)	0 / 18 (0.00%)
occurrences (all)	2	6	0
Dysgeusia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Headache			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Seizure			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 22 (54.55%)	14 / 22 (63.64%)	10 / 18 (55.56%)
occurrences (all)	14	20	15
Hypercoagulation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Hyperfibrinogenaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Leukopenia			

subjects affected / exposed	2 / 22 (9.09%)	4 / 22 (18.18%)	2 / 18 (11.11%)
occurrences (all)	4	9	7
Lymphopenia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Neutropenia			
subjects affected / exposed	3 / 22 (13.64%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	4	1	3
Thrombocytosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	9 / 22 (40.91%)	8 / 22 (36.36%)	5 / 18 (27.78%)
occurrences (all)	12	10	9
Colitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			

subjects affected / exposed	3 / 22 (13.64%)	5 / 22 (22.73%)	4 / 18 (22.22%)
occurrences (all)	3	7	4
Dysphagia			
subjects affected / exposed	3 / 22 (13.64%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	3	2	0
Dyspepsia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Haemorrhoids			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gingival swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 22 (13.64%)	0 / 22 (0.00%)	5 / 18 (27.78%)
occurrences (all)	3	0	5
Nausea			
subjects affected / exposed	6 / 22 (27.27%)	11 / 22 (50.00%)	7 / 18 (38.89%)
occurrences (all)	7	18	8
Odynophagia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			
subjects affected / exposed	4 / 22 (18.18%)	4 / 22 (18.18%)	4 / 18 (22.22%)
occurrences (all)	4	4	4
Paraesthesia oral			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Stomatitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Toothache			

subjects affected / exposed	1 / 22 (4.55%)	3 / 22 (13.64%)	0 / 18 (0.00%)
occurrences (all)	1	4	0
Vomiting			
subjects affected / exposed	2 / 22 (9.09%)	4 / 22 (18.18%)	1 / 18 (5.56%)
occurrences (all)	2	5	1
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 22 (13.64%)	7 / 22 (31.82%)	4 / 18 (22.22%)
occurrences (all)	3	7	5
Dermal cyst			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Decubitus ulcer			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Angioedema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Dry skin			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	2 / 18 (11.11%)
occurrences (all)	1	2	3
Papule			

subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pain of skin			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Night sweats			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	4 / 22 (18.18%)	2 / 22 (9.09%)	2 / 18 (11.11%)
occurrences (all)	5	2	2
Skin exfoliation			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	3 / 22 (13.64%)	4 / 22 (18.18%)	1 / 18 (5.56%)
occurrences (all)	3	4	1
Thyroid mass			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Thyroiditis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Osteoporotic fracture			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	3 / 22 (13.64%)	3 / 22 (13.64%)	2 / 18 (11.11%)
occurrences (all)	3	5	2
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	3 / 18 (16.67%)
occurrences (all)	1	4	3
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Body tinea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 22 (0.00%)	4 / 22 (18.18%)	2 / 18 (11.11%)
occurrences (all)	0	4	2
COVID-19 pneumonia			

subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Diarrhoea infectious			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
External ear cellulitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	2	4	0
Oral fungal infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	4 / 18 (22.22%)
occurrences (all)	2	1	5
Pneumonia pseudomonal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	3 / 22 (13.64%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Sinusitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Suspected COVID-19			

subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	4 / 18 (22.22%)
occurrences (all)	1	2	5
Urinary tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Folate deficiency			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Electrolyte imbalance			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Decreased appetite			
subjects affected / exposed	7 / 22 (31.82%)	7 / 22 (31.82%)	5 / 18 (27.78%)
occurrences (all)	8	9	7
Glucose tolerance impaired			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	1	1	2
Hypertriglyceridaemia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	1 / 18 (5.56%)
occurrences (all)	2	3	5
Hyperphosphataemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Hypermagnesaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Hyperlipidaemia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Hyperkalaemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
Hyperglycaemia			
subjects affected / exposed	5 / 22 (22.73%)	4 / 22 (18.18%)	1 / 18 (5.56%)
occurrences (all)	14	8	1
Hypochloraemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	1 / 22 (4.55%)	4 / 22 (18.18%)	3 / 18 (16.67%)
occurrences (all)	1	5	3
Hypomagnesaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	1 / 22 (4.55%)	3 / 22 (13.64%)	1 / 18 (5.56%)
occurrences (all)	4	3	1
Hypoalbuminaemia			
subjects affected / exposed	5 / 22 (22.73%)	7 / 22 (31.82%)	6 / 18 (33.33%)
occurrences (all)	6	11	9
Hyperuricaemia			
subjects affected / exposed	3 / 22 (13.64%)	3 / 22 (13.64%)	4 / 18 (22.22%)
occurrences (all)	7	8	6
Hyponatraemia			
subjects affected / exposed	5 / 22 (22.73%)	6 / 22 (27.27%)	5 / 18 (27.78%)
occurrences (all)	6	11	13
Hypophosphataemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hypoproteinaemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	0 / 18 (0.00%)
occurrences (all)	1	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 April 2021	Protocol Amendment 1.0
21 April 2022	Protocol Amendment 2.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Since no participants were enrolled under PA 2, no analyses of the primary or secondary endpoints were conducted. Participants enrolled under PA 1 were excluded from the primary and secondary analyses outlined for PA 2.

Notes: