Clinical trial results:
A Randomized, Controlled, Open-label, Global Phase 3 Study Comparing the Efficacy of the anti-PD-1 Antibody BGB-A317 versus Chemotherapy as Second Line Treatment in Patients with Advanced Unresectable/Metastatic Esophageal Squamous Cell Carcinoma

Summary

EudraCT number	2017-003699-30
Trial protocol	DE FR ES IT GB BE
Global end of trial date	28 December 2022

Results information

Result version number	v1 (current)
This version publication date	26 November 2023
First version publication date	26 November 2023

Trial information

Trial identification

Sponsor protocol code	BGB-A317-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03430843
WHO universal trial number (UTN)	-
Other trial identifiers	ChinaDrugTrials : CTR20171026 , IND: 135699

Notes:

Sponsors

Sponsor organisation name	BeiGene, Ltd., c/o BeiGene USA, Inc.
Sponsor organisation address	1840 Gateway Drive, Third Floor, San Mateo, United States, 94404
Public contact	BeiGene Clinical Support, BeiGene, Ltd., clinicaltrials@beigene.com
Scientific contact	BeiGene Clinical Support, BeiGene, Ltd., 1 8778285568, 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	22 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the overall survival (OS) following treatment with BGB-A317 vs. investigator chosen chemotherapy (ICC) when given as second line treatment in patients with advanced unresectable/metastatic Esophageal Squamous Cell Carcinoma (ESCC)

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	26 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	China: 296
Country: Number of subjects enrolled	Taiwan: 27
Country: Number of subjects enrolled	Japan: 50
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 31
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	512
EEA total number of subjects	88

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)	310
From 65 to 84 years	201
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 132 study centers in Mainland China, Taiwan, United States, France, Italy, Germany, Spain, Japan, South Korea, Belgium and the United Kingdom.

Pre-assignment

Screening details:

The study was composed of an initial screening phase (up to 28 days), a treatment phase, a safety follow-up phase (including Safety Follow-up Visit), and a survival follow-up phase.

Period 1

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

Blinding implementation details:

randomized, controlled, open-label study

Arms

Are arms mutually exclusive?	Yes
Arm title	Tislelizumab

Arm description:

Tislelizumab 200 mg intravenously (IV) on Day 1 every 21 days until disease progression, unacceptable toxicity, or other discontinuation criteria were met.

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

Dosage and administration details:

Tislelizumab 200 mg administered intravenously once every 3 weeks

Arm title	Investigator Chosen Chemotherapy (ICC)

Arm description:

Investigator choice of either paclitaxel 135-175 mg /m² on Day 1 IV every 21 days or 80-100 mg/m^2 on a weekly schedule; docetaxel 75 mg/m^2 IV on Day 1 every 21 days; or irinotecan 125 mg/m^2 IV on Days 1 and 8 every 21 days

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

Dosage and administration details:

Paclitaxel 135-175 mg /m² administered IV given every 21 days, or 80-100mg/m2 administered IV weekly

Number of subjects in period 1	Tislelizumab	Investigator Chosen Chemotherapy (ICC)
Started	256	256
Treated	255	240
Completed	0	0
Not completed	256	256
Consent withdrawn by subject	5	14
Subject Death	233	233
Sponsor Decision	17	6
Lost to follow-up	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Tislelizumab
Reporting group description:	
Tislelizumab 200 mg intravenously (IV) on Day 1 every 21 days until disease progression, unacceptable toxicity, or other discontinuation criteria were met.	
Reporting group title	Investigator Chosen Chemotherapy (ICC)
Reporting group description:	
Investigator choice of either paclitaxel 135-175 mg /m² on Day 1 IV every 21 days or 80-100 mg/m^2 on a weekly schedule; docetaxel 75 mg/m^2 IV on Day 1 every 21 days; or irinotecan 125 mg/m^2 IV on Days 1 and 8 every 21 days	

Reporting group values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)	Total
Number of subjects	256	256	512
Age categorical			
Unit of measure: participants			
Units: Subjects			
<65 years	152	158	310
> 65 years	104	98	202
Age continuous			
Mean (Standard Deviation)			
Units: years			
arithmetic mean	61.8	61.8	
standard deviation	± 8.41	± 8.02	-
Gender categorical			
Measure Type: Count of Participants			
Units: Subjects			
Female	39	41	80
Male	217	215	432
Race Units: Subjects			
Asian	201	207	408
White or Caucasian	53	44	97
Not Reported	1	0	1
Unknown	1	2	3
Black of African American	0	2	2
Other	0	1	1
Eastern Cooperative Oncology Group (ECOG) Performance Status Score			
Measure Description: Measure Description: ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity)			
Units: Subjects			
Zero	66	61	127

One	190	195	385
PD-L1 Expression Status			
Measure Description: Programmed death ligand 1 (PD-L1) positive is defined as visually-estimated Combined Positive Score (vCPS) >= 10%, PD-L1 negative is defined as vCPS < 10%, PD-L1 missing refers to the participants without sample collection, not evaluable at baseline, or scored with unqualified sample. Note terminology was updated from vCPS to Tumor Area Positivity (TAP) score in manuscripts.			
Units: Subjects			
vCPS greater than or equal to 10%	80	62	142
vCPS less than 10%	100	122	222
Missing	76	72	148

End points

End points reporting groups

Reporting group title	Tislelizumab
Reporting group description:	
Tislelizumab 200 mg intravenously (IV) on Day 1 every 21 days until disease progression, unacceptable toxicity, or other discontinuation criteria were met.	
Reporting group title	Investigator Chosen Chemotherapy (ICC)
Reporting group description:	
Investigator choice of either paclitaxel 135-175 mg /m² on Day 1 IV every 21 days or 80-100 mg/m^2 on a weekly schedule; docetaxel 75 mg/m^2 IV on Day 1 every 21 days; or irinotecan 125 mg/m^2 IV on Days 1 and 8 every 21 days	

Primary: Overall survival (OS) in the Intent-to-Treat (ITT) Analysis Set

End point title	Overall survival (OS) in the Intent-to-Treat (ITT) Analysis Set
End point description:	
OS is defined as the length of time from the date of randomization until the date of death due to any cause in all randomized participants The ITT analysis set included all randomized participants.	
End point type	Primary
End point timeframe:	
Approximately 2 years and 10 months from date of first randomization	

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	256		
Units: Months				
median (confidence interval 95%)	8.6 (7.5 to 10.4)	6.3 (5.3 to 7.0)		

Statistical analyses

Statistical analysis title	Superiority
Comparison groups	Tislelizumab v Investigator Chosen Chemotherapy (ICC)
Number of subjects included in analysis	512
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	1-sided, Log Rank Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.85

Secondary: Overall survival (OS) in the PDL-1 Positive Analysis Set

End point title	Overall survival (OS) in the PDL-1 Positive Analysis Set

End point description:

OS is defined as the time from the date of randomization until the date of death due to any cause in the PD-L1 positive population, defined as vCPS ≥10%. The PD-L1 positive population included all randomized participants with tumor PD-L1 vCPS ≥10%.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	62		
Units: Months				
median (confidence interval 95%)	10.2 (8.5 to 14.5)	5.1 (3.8 to 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR) in the ITT analysis set

End point title	Objective response rate (ORR) in the ITT analysis set

End point description:

ORR is defined as the percentage of participants who had complete response (CR) or partial response (PR) as assessed by the investigator per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; The ITT analysis set included all randomized participants.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	256		
Units: Percentage of Participants				
number (confidence interval 95%)	20.3 (15.6 to 25.8)	9.8 (6.4 to 14.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) in the PD-L1 Positive Analysis Set

End point title	Overall Response Rate (ORR) in the PD-L1 Positive Analysis Set

End point description:

ORR is defined as the percentage of participants who had complete response (CR) or partial response (PR) as assessed by the investigator per RECIST v1.1. The PD-L1 positive population is defined as a visually-estimated combined positive score (vCPS) ≥10%

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	62		
Units: Percentage of Participants				
number (confidence interval 95%)	26.3 (17 to 37.3)	11.3 (4.7 to 21.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) in the ITT Analysis Set

End point title	Progression-free Survival (PFS) in the ITT Analysis Set

End point description:

PFS is defined as the time from the date of randomization to the date of first documentation of disease progression assessed by the investigator per RECIST v1.1 or death, whichever occurs first; reported for the ITT analysis set.
The ITT analysis set included all randomized participants

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	256		
Units: Months				
median (confidence interval 95%)	1.6 (1.4 to 2.7)	2.1 (1.5 to 2.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) in the PDL-1 Positive Analysis Set

End point title	Progression-free Survival (PFS) in the PDL-1 Positive Analysis Set

End point description:

PFS is defined as the time from the date of randomization to the date of first documentation of disease progression assessed by the investigator per RECIST v1.1 or death, whichever occurs first; reported for the PDL-1 Positive Analysis Set. The PD-L1 positive population is defined as a visually-estimated combined positive score (vCPS) ≥10%.

End point type	Secondary

End point timeframe:

Up to 2 years and 10 months from date of first randomization

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	62		
Units: Months				
median (confidence interval 95%)	2.7 (1.5 to 4.2)	2.3 (1.4 to 3.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) in the ITT Analysis Set

End point title	Duration of Response (DOR) in the ITT Analysis Set

End point description:

DOR is defined as the time from the first determination of an objective response until the first

documentation of progression as assessed by the investigator per RECIST v1.1, or death, whichever comes first. The ITT analysis set included all randomized participants; only participants with an objective response (CR or PR) were included in this analysis.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	25		
Units: Months				
median (confidence interval 95%)	7.1 (4.1 to 11.3)	4.0 (2.1 to 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) in the PDL-1 Positive Analysis Set

End point title	Duration of Response (DOR) in the PDL-1 Positive Analysis Set

End point description:

DOR is defined as the time from the first determination of an objective response until the first documentation of progression as assessed by the investigator per RECIST v1.1, or death, whichever comes first. The PD-L1 positive population is defined as a visually estimated combined positive score (vCPS) ≥10%; only participants with an objective response (CR or PR) were included in this analysis.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	7[1]		
Units: Months				
median (confidence interval 95%)	7.1 (2.9 to 13.2)	5.7 (1.2 to 9999)		

Notes:

[1] - 9999 = Not estimable due to insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Health-Related Quality of Life (HRQoL) as Assessed by European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C-30) in the ITT analysis set

End point title	Health-Related Quality of Life (HRQoL) as Assessed by European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C-30) in the ITT analysis set

End point description:

Mean change from baseline in EORTC QLQ-C30 index score. The EORTC QLQ-C30 v3.0 is a questionnaire that assesses quality of life of cancer participants. 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.

The ITT analysis set included all randomized participants; "Overall number of participants analyzed" refers to number of participants evaluable for this outcome measure and "Number analyzed" refers to participants evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	246		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline; n=239; n=246	16.2 (± 12.28)	18.3 (± 13.86)		
Change at Cycle 6; n=98; n=36	0.2 (± 8.28)	4.8 (± 9.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL as Assessed by EORTC QLQ-C30 in the PDL-1 Positive Analysis Set

End point title	HRQoL as Assessed by EORTC QLQ-C30 in the PDL-1 Positive Analysis Set

End point description:

Mean change from baseline in EORTC QLQ-C30 index score. The EORTC QLQ-C30 v3.0 is a questionnaire that assesses quality of life of cancer participants. 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.

The PD-L1 positive population is defined as a visually estimated combined positive score (vCPS) ≥10%; "Overall number of participants analyzed" refers to number of participants evaluable for this outcome measure and "Number analyzed" refers to participants evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	59		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline; n=77; n=59	16.8 (± 10.96)	18.8 (± 12.02)		
Change at Cycle 6; n=39; n=9	0.5 (± 7.39)	0.5 (± 4.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL as Assessed by EORTC QLQ-Oesophagus Cancer Module (EORTC QLQ-OES18) Reported in ITT Analysis Set

End point title	HRQoL as Assessed by EORTC QLQ-Oesophagus Cancer Module (EORTC QLQ-OES18) Reported in ITT Analysis Set

End point description:

Mean change from baseline in EORTC QLQ-OES18 index score. The EORTC QLQ-OES18 is a questionnaire that assesses overall symptoms in esophageal cancer participants. It includes 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. The ITT analysis set included all randomized participants; "Overall number of participants analyzed" refers to number of participants evaluable for this outcome measure and "Number analyzed" refers to participants evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline to Cycle 6 Day 1 (each cycle is 21 days)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	246		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	14.7 (± 11.81)	16.3 (± 13.20)		
Change at Cycle 6	-0.6 (± 8.63)	3.0 (± 12.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL as Assessed by EORTC QLQ-OES18) in the PDL-1 Positive Analysis Set.

End point title	HRQoL as Assessed by EORTC QLQ-OES18) in the PDL-1 Positive Analysis Set.

End point description:

Mean change from baseline in EORTC QLQ-OES18 index score. The EORTC QLQ-OES18 is a questionnaire that assesses overall symptoms in esophageal cancer participants. It includes 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. The PD-L1 positive population is defined as a visually-estimated combined positive score (vCPS) ≥10%; "Overall number of participants analyzed" refers to number of participants evaluable for this outcome measure and "Number analyzed" refers to participants evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline to Cycle 6 Day 1 (each cycle is 21 days)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	59		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	16.5 (± 12.69)	18.1 (± 12.21)		
Change at Cycle 6	-0.9 (± 7.45)	-2.9 (± 5.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL as Assessed by European Quality of Life 5-Dimensions 5-Level Questionnaire (EQ-5D-5L) in the ITT Analysis Set

End point title	HRQoL as Assessed by European Quality of Life 5-Dimensions 5-Level Questionnaire (EQ-5D-5L) in the ITT Analysis Set

End point description:

Mean change from baseline in EQ-5D-5L visual acuity score (VAS). The EQ-5D-5L measures health outcomes using a VAS to record a participant's self-rated health on a scale from 0 to 100, where 100 is 'the best health you can imagine' and 0 is 'the worst health you can imagine.' A higher score indicates better health outcomes.

The ITT analysis set included all randomized participants; "Overall number of participants analyzed" refers to number of participants evaluable for this outcome measure and "Number analyzed" refers to participants evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	247		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	73.7 (± 17.05)	72.5 (± 18.13)		
Change at Cycle 6	-0.6 (± 14.81)	-5.9 (± 16.34)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL as Assessed by EQ-5D-5L in the PD-L1 Positive Analysis Set

End point title	HRQoL as Assessed by EQ-5D-5L in the PD-L1 Positive Analysis Set

End point description:

Mean change from baseline in EQ-5D-5L visual acuity score (VAS). The EQ-5D-5L measures health outcomes using a VAS to record a participant's self-rated health on a scale from 0 to 100, where 100 is 'the best health you can imagine' and 0 is 'the worst health you can imagine.' A higher score indicates better health outcomes.

The PD-L1 positive population is defined as a visually-estimated combined positive score (vCPS) ≥10%; "Overall number of participants analyzed" refers to number of participants evaluable for this outcome measure and "Number analyzed" refers to participants evaluable at the specified time point

End point type	Secondary

End point timeframe:

Through End-of-Trial Analysis data cutoff date of 28-Dec-2022 (up to approximately 5 years)

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	59		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	74.1 (± 14.84)	70.5 (± 18.40)		
Change at Cycle 6	-0.5 (± 17.59)	4.4 (± 12.82)		

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), which includes laboratory tests, physical exams, electrocardiogram results and vital signs

End point type	Secondary

End point timeframe:

From the first dose date to 30 days after the last dose date; up to approximately 4 years and 11 months

End point values	Tislelizumab	Investigator Chosen Chemotherapy (ICC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	240		
Units: Number of Participants				
Number of participants with TEAEs	245	236		
Number of participants with SAEs	109	106		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse events (AEs): up to approximately 4 years and 11 months

Adverse event reporting additional description:

AEs are defined as events that had an onset date or a worsening in severity from baseline (pretreatment) on or after the first dose of study treatment up to 30 days following study treatment discontinuation or initiation of a new anticancer therapy, whichever occurred first.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Investigator Chosen Therapy (ICC)

Reporting group description:

Investigator choice of either paclitaxel 135-175 mg /m² on Day 1 IV every 21 days or 80-100 mg/m^2 on a weekly schedule; docetaxel 75 mg/m^2 IV on Day 1 every 21 days; or irinotecan 125 mg/m^2 IV on Days 1 and 8 every 21 days

Reporting group title	Tislelizumab

Reporting group description:

Tislelizumab 200 mg intravenously (IV) on Day 1 every 21 days until disease progression, unacceptable toxicity, or other discontinuation criteria were met.

Serious adverse events	Investigator Chosen Therapy (ICC)	Tislelizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	106 / 240 (44.17%)	109 / 255 (42.75%)	
number of deaths (all causes)	233	233	
number of deaths resulting from adverse events	28	35	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 240 (0.42%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	2 / 240 (0.83%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Tumour fistulisation			

subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour compression			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to heart			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	4 / 240 (1.67%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	1 / 4	0 / 2	
Fatigue			
subjects affected / exposed	0 / 240 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	4 / 240 (1.67%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	2 / 5	0 / 3	
deaths causally related to treatment / all	2 / 5	0 / 3	
Malaise			
subjects affected / exposed	2 / 240 (0.83%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 240 (0.42%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 4	
deaths causally related to treatment / all	1 / 1	1 / 4	
Oedema peripheral			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 240 (0.83%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Immune system disorders			

Anaphylactic shock			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 240 (0.42%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemoptysis			
subjects affected / exposed	2 / 240 (0.83%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Immune-mediated lung disease			
subjects affected / exposed	0 / 240 (0.00%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophagobronchial fistula			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pleural effusion			
subjects affected / exposed	4 / 240 (1.67%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonitis			
subjects affected / exposed	2 / 240 (0.83%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	1 / 2	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	6 / 6	
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	4 / 240 (1.67%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchiectasis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pulmonary embolism			
subjects affected / exposed	1 / 240 (0.42%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 240 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			

subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Tracheal stenosis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal fistula			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	8 / 240 (3.33%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	11 / 11	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Neutrophil count decreased			
subjects affected / exposed	10 / 240 (4.17%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	14 / 14	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Thoracic vertebral fracture			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal haemorrhage			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheostomy malfunction			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune-mediated myocarditis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Autoimmune myocarditis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cerebral infarction			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			

subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	3 / 240 (1.25%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	5 / 9	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	8 / 240 (3.33%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	9 / 9	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	4 / 240 (1.67%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	7 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 240 (0.83%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	8 / 240 (3.33%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	8 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric fistula			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	2 / 240 (0.83%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			

subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal distension			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	4 / 240 (1.67%)	13 / 255 (5.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal obstruction			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagomediastinal fistula			

subjects affected / exposed	0 / 240 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			
subjects affected / exposed	0 / 240 (0.00%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal fistula			
subjects affected / exposed	1 / 240 (0.42%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Odynophagia			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	4 / 240 (1.67%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal obstruction			

subjects affected / exposed	1 / 240 (0.42%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	0 / 1	2 / 6	
deaths causally related to treatment / all	0 / 0	2 / 2	
Reflux gastritis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	4 / 240 (1.67%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	1 / 4	1 / 4	
deaths causally related to treatment / all	0 / 1	1 / 3	
Vomiting			
subjects affected / exposed	3 / 240 (1.25%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	3 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephroangiosclerosis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenocorticotropic hormone deficiency			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated myositis			
subjects affected / exposed	0 / 240 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			

subjects affected / exposed	1 / 240 (0.42%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pathological fracture			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess neck			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peritonitis			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	2 / 240 (0.83%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular abscess			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	4 / 240 (1.67%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	4 / 4	0 / 2	
deaths causally related to treatment / all	3 / 3	0 / 0	
Sepsis			
subjects affected / exposed	1 / 240 (0.42%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory tract infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 240 (0.42%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	17 / 240 (7.08%)	19 / 255 (7.45%)	
occurrences causally related to treatment / all	6 / 18	10 / 24	
deaths causally related to treatment / all	1 / 3	2 / 6	
Pneumonia bacterial			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 240 (2.50%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	3 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 240 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			

subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 240 (0.00%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 0	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 240 (0.42%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochloraemia			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 240 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 240 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Investigator Chosen Therapy (ICC)	Tislelizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	231 / 240 (96.25%)	232 / 255 (90.98%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 240 (1.25%)	10 / 255 (3.92%)	
occurrences (all)	4	12	
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 240 (2.50%)	10 / 255 (3.92%)	
occurrences (all)	8	14	
Hypertension			
subjects affected / exposed	6 / 240 (2.50%)	13 / 255 (5.10%)	
occurrences (all)	15	32	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	33 / 240 (13.75%)	40 / 255 (15.69%)	
occurrences (all)	42	56	
Oedema peripheral			
subjects affected / exposed	11 / 240 (4.58%)	9 / 255 (3.53%)	
occurrences (all)	13	12	
Malaise			
subjects affected / exposed	35 / 240 (14.58%)	16 / 255 (6.27%)	
occurrences (all)	54	18	
Fatigue			
subjects affected / exposed	42 / 240 (17.50%)	33 / 255 (12.94%)	
occurrences (all)	68	43	
Asthenia			
subjects affected / exposed	36 / 240 (15.00%)	29 / 255 (11.37%)	
occurrences (all)	63	41	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	28 / 240 (11.67%)	44 / 255 (17.25%)	
occurrences (all)	30	56	
Dysphonia			
subjects affected / exposed	2 / 240 (0.83%)	8 / 255 (3.14%)	
occurrences (all)	2	8	
Dyspnoea			
subjects affected / exposed	19 / 240 (7.92%)	25 / 255 (9.80%)	
occurrences (all)	23	29	
Pneumonitis			
subjects affected / exposed	2 / 240 (0.83%)	10 / 255 (3.92%)	
occurrences (all)	2	12	
Productive cough			
subjects affected / exposed	18 / 240 (7.50%)	18 / 255 (7.06%)	
occurrences (all)	19	21	
Haemoptysis			
subjects affected / exposed	5 / 240 (2.08%)	10 / 255 (3.92%)	
occurrences (all)	7	11	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	17 / 240 (7.08%)	21 / 255 (8.24%)	
occurrences (all)	23	24	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	19 / 240 (7.92%)	33 / 255 (12.94%)	
occurrences (all)	22	49	
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 240 (4.58%)	37 / 255 (14.51%)	
occurrences (all)	13	55	
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 240 (2.08%)	17 / 255 (6.67%)	
occurrences (all)	10	26	
Blood bilirubin increased			
subjects affected / exposed	6 / 240 (2.50%)	9 / 255 (3.53%)	
occurrences (all)	11	16	
Blood creatine phosphokinase MB increased			

subjects affected / exposed	1 / 240 (0.42%)	11 / 255 (4.31%)	
occurrences (all)	1	14	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 240 (0.00%)	10 / 255 (3.92%)	
occurrences (all)	0	15	
C-reactive protein increased			
subjects affected / exposed	2 / 240 (0.83%)	8 / 255 (3.14%)	
occurrences (all)	2	8	
Gamma-glutamyltransferase increased			
subjects affected / exposed	8 / 240 (3.33%)	14 / 255 (5.49%)	
occurrences (all)	10	23	
Lymphocyte count decreased			
subjects affected / exposed	22 / 240 (9.17%)	12 / 255 (4.71%)	
occurrences (all)	36	21	
Neutrophil count decreased			
subjects affected / exposed	88 / 240 (36.67%)	6 / 255 (2.35%)	
occurrences (all)	202	19	
Platelet count decreased			
subjects affected / exposed	16 / 240 (6.67%)	14 / 255 (5.49%)	
occurrences (all)	20	23	
Weight decreased			
subjects affected / exposed	45 / 240 (18.75%)	62 / 255 (24.31%)	
occurrences (all)	55	101	
White blood cell count decreased			
subjects affected / exposed	95 / 240 (39.58%)	11 / 255 (4.31%)	
occurrences (all)	227	25	
White blood cell count increased			
subjects affected / exposed	6 / 240 (2.50%)	12 / 255 (4.71%)	
occurrences (all)	8	17	
Nervous system disorders			
Dizziness			
subjects affected / exposed	19 / 240 (7.92%)	11 / 255 (4.31%)	
occurrences (all)	26	13	
Peripheral sensory neuropathy			

subjects affected / exposed	23 / 240 (9.58%)	2 / 255 (0.78%)	
occurrences (all)	36	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	109 / 240 (45.42%)	80 / 255 (31.37%)	
occurrences (all)	192	139	
Thrombocytopenia			
subjects affected / exposed	10 / 240 (4.17%)	5 / 255 (1.96%)	
occurrences (all)	13	7	
Neutropenia			
subjects affected / exposed	30 / 240 (12.50%)	2 / 255 (0.78%)	
occurrences (all)	56	11	
Leukopenia			
subjects affected / exposed	29 / 240 (12.08%)	9 / 255 (3.53%)	
occurrences (all)	57	19	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	45 / 240 (18.75%)	41 / 255 (16.08%)	
occurrences (all)	60	46	
Abdominal pain upper			
subjects affected / exposed	16 / 240 (6.67%)	9 / 255 (3.53%)	
occurrences (all)	18	12	
Abdominal pain			
subjects affected / exposed	22 / 240 (9.17%)	17 / 255 (6.67%)	
occurrences (all)	27	20	
Abdominal distension			
subjects affected / exposed	8 / 240 (3.33%)	9 / 255 (3.53%)	
occurrences (all)	9	10	
Stomatitis			
subjects affected / exposed	14 / 240 (5.83%)	9 / 255 (3.53%)	
occurrences (all)	21	10	
Nausea			
subjects affected / exposed	72 / 240 (30.00%)	37 / 255 (14.51%)	
occurrences (all)	123	43	
Gastrooesophageal reflux disease			

subjects affected / exposed	12 / 240 (5.00%)	14 / 255 (5.49%)	
occurrences (all)	13	16	
Dysphagia			
subjects affected / exposed	17 / 240 (7.08%)	22 / 255 (8.63%)	
occurrences (all)	22	23	
Diarrhoea			
subjects affected / exposed	75 / 240 (31.25%)	32 / 255 (12.55%)	
occurrences (all)	134	47	
Vomiting			
subjects affected / exposed	48 / 240 (20.00%)	27 / 255 (10.59%)	
occurrences (all)	88	33	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	42 / 240 (17.50%)	1 / 255 (0.39%)	
occurrences (all)	46	1	
Pruritus			
subjects affected / exposed	11 / 240 (4.58%)	25 / 255 (9.80%)	
occurrences (all)	13	34	
Rash			
subjects affected / exposed	10 / 240 (4.17%)	23 / 255 (9.02%)	
occurrences (all)	10	31	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 240 (0.42%)	8 / 255 (3.14%)	
occurrences (all)	1	8	
Hypothyroidism			
subjects affected / exposed	1 / 240 (0.42%)	30 / 255 (11.76%)	
occurrences (all)	1	37	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 240 (7.50%)	22 / 255 (8.63%)	
occurrences (all)	24	25	
Back pain			
subjects affected / exposed	17 / 240 (7.08%)	28 / 255 (10.98%)	
occurrences (all)	27	32	
Myalgia			

subjects affected / exposed	14 / 240 (5.83%)	8 / 255 (3.14%)	
occurrences (all)	26	9	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 240 (2.50%)	9 / 255 (3.53%)	
occurrences (all)	7	14	
Pneumonia			
subjects affected / exposed	14 / 240 (5.83%)	28 / 255 (10.98%)	
occurrences (all)	17	31	
Upper respiratory tract infection			
subjects affected / exposed	11 / 240 (4.58%)	8 / 255 (3.14%)	
occurrences (all)	11	11	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	80 / 240 (33.33%)	42 / 255 (16.47%)	
occurrences (all)	102	53	
Hyperglycaemia			
subjects affected / exposed	8 / 240 (3.33%)	17 / 255 (6.67%)	
occurrences (all)	8	35	
Hyperkalaemia			
subjects affected / exposed	2 / 240 (0.83%)	8 / 255 (3.14%)	
occurrences (all)	3	13	
Hyperuricaemia			
subjects affected / exposed	11 / 240 (4.58%)	6 / 255 (2.35%)	
occurrences (all)	19	13	
Hypoalbuminaemia			
subjects affected / exposed	30 / 240 (12.50%)	36 / 255 (14.12%)	
occurrences (all)	44	51	
Hypocalcaemia			
subjects affected / exposed	11 / 240 (4.58%)	8 / 255 (3.14%)	
occurrences (all)	17	11	
Hypochloraemia			
subjects affected / exposed	10 / 240 (4.17%)	6 / 255 (2.35%)	
occurrences (all)	13	10	
Hypoglycaemia			

subjects affected / exposed	3 / 240 (1.25%)	8 / 255 (3.14%)	
occurrences (all)	4	11	
Hypokalaemia			
subjects affected / exposed	22 / 240 (9.17%)	22 / 255 (8.63%)	
occurrences (all)	42	23	
Hyponatraemia			
subjects affected / exposed	33 / 240 (13.75%)	31 / 255 (12.16%)	
occurrences (all)	45	56	
Hypoproteinaemia			
subjects affected / exposed	8 / 240 (3.33%)	13 / 255 (5.10%)	
occurrences (all)	10	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2017	Evaluation of objective response rate, progression-free survival, and duration of response using immune-related RECIST was removed because the tool had not been validated. The stratification factors were modified (gender was replaced with ECOG PS score and ICC option) per the request from the US FDA. Alternative paclitaxel and docetaxel treatment regimens were added to provide Japan-specific regimens per the request from the PMDA. Clarified that patients who had received ≥ 2 prior systemic treatments for advanced unresectable or metastatic ESCC were excluded. Management guidance for infusion-related reactions, severe hypersensitivity reactions, flu-like symptoms, and renal function abnormalities were added. The guidance for the immune-mediated adverse event management was modified and updated
06 December 2017	The requirement of treatment beyond radiographic progression was further clarified per the request from the US FDA. Criteria for dose modification of paclitaxel, docetaxel and irinotecan and permanent discontinuation of chemotherapy regimens were clarified, and dose modifications guidelines for specific adverse events and other toxicities were provided, per request from the US FDA
08 November 2018	CK (creatine kinase) and CK-MB (creatine kinase cardiac muscle isoenzyme) tests and management guidance were added to monitor the risk of myocarditis more closely. Incorporated the US FDA request of implementing measures to further decrease the potential for viral reactivation: Continuous treatment for 6 months after treatment discontinuation was required for patients with detectable HbsAg or HBV DNA; continuous effective antiviral therapy was required for patients who had detectable HCV and were receiving treatment at screening. The criterion to exclude patients who had a history of anterior organ transplant, including stem-cell allograft, was added per the request from the French National Agency for the Safety of Medicines and Health Products (ANSM). Immune-mediated adverse event management guidelines were updated: "Tislelizumab must be permanently discontinued for any onset of Grade 4 or recurrent Grade 3 immune-mediated adverse events." A new appendix of "Determining Line of Therapy in ESCC" was added to further clarify the definition of first-line systemic treatment in inclusion criteria, and first-line or front-line systemic treatment was defined as "platinum-based regimen."

20 March 2020	Updated the statistical estimation of the sample size to increase the sample size from 450 to 500 and increase target number of death events from 336 to 400, with the following consideration: (1) overall survival HR was adjusted from 0.73 to 0.75 based on recently published results of anti-PD-1 therapies in second-line treatment of ESCC and (2) addition of a dropout rate of 5%. The predefined interim analysis was removed due to the lack of geographically representative population for the analysis, which resulted from the disparity in global enrollment rates. The overall survival in patients with PD-L1 vCPS ≥ 10% was added as the key secondary endpoint of this study to reflect the clinical relevance and importance of the PD-L1 biomarker in ESCC observed in competitors' published data. (Note: PD-L1 assessment [by VENTANA PD-L1 SP263 CDx Assay] was not started before the key secondary endpoint was added in this protocol amendment, and PD-L1 status of each patient was unknown.)
20 July 2020	Provided definition of the predefined cutoff for the PD-L1-Positive Analysis Set. Added details for management of Grade 3 myositis/rhabdomyolysis in Appendix 10 of Study 302 Protocol Amendment Version 4.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35442766