

**Clinical trial results:****A Phase 2, Multicenter, Randomized, Placebo-Controlled Study to Compare the Efficacy of Anti-PD-1 Monoclonal Antibody Tislelizumab (BGB-A317) Plus Anti-TIGIT Monoclonal Antibody Ociperlimab (BGB-A1217) Versus Tislelizumab Plus Placebo as Second-Line Treatment in Patients With PD-L1 Tumor Area Positivity (TAP) 10% Unresectable, Locally Advanced, Recurrent or Metastatic Esophageal Squamous Cell Carcinoma****Summary**

EudraCT number	2020-004658-32
Trial protocol	FR ES
Global end of trial date	26 December 2023

Results information

Result version number	v1 (current)
This version publication date	08 January 2025
First version publication date	08 January 2025

Trial information**Trial identification**

Sponsor protocol code	BGB-A317-A1217-203
-----------------------	--------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04732494
WHO universal trial number (UTN)	-
Other trial identifiers	ChinaDrugTrials.org: CTR20213241/CTR20210243, BeiGene: AdvanTIG-203

Notes:

Sponsors

Sponsor organisation name	BeiGene
Sponsor organisation address	1840 Gateway Drive, San Mateo, CA, United States, 94404
Public contact	Clinical Trial Information Email, BeiGene USA, Inc., 1 877-828-5568, ClinicalTrials@beigene.com
Scientific contact	Clinical Trial Information Email, 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	26 December 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the objective response rate (ORR) as assessed by the investigator according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1), of tislelizumab plus ociperlimab with tislelizumab plus placebo as second-line treatment in patients with programmed cell death ligand-1 (PD-L1) tumor area positivity (TAP) $\geq 10\%$ unresectable, locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC).

Protection of trial subjects:

This study was conducted in accordance with BeiGene, Ltd. (BeiGene) procedures, which comply with the principles of Good Clinical Practice, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines, the Declaration of Helsinki, and applicable local regulatory requirements.

The protocol, protocol amendments, and informed consent forms (ICFs) were reviewed and approved by the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) in conformance with Good Clinical Practice and applicable regulatory requirements.

The IEC/IRB-approved ICF was signed and dated by the patient or the patient's legally authorized representative before his or her participation in the study. A copy of each signed ICF was provided to the patient or the patient's legally authorized representative.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 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: 73
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Taiwan: 20
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	France: 6
Worldwide total number of subjects	125
EEA total number of subjects	13

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)	67
From 65 to 84 years	58
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 52 study centers in 7 countries (Chinese mainland, Chinese Taiwan, South Korea, Thailand, France, Spain, and Russia).

Pre-assignment

Screening details:

Participants were randomized equally to one of two treatment groups. Randomization was stratified by Eastern Cooperative Oncology Group Performance Status (ECOG PS) score (0 versus 1), number of organs with metastases (≤ 1 versus ≥ 2), and region (Asia versus non-Asia).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Tislelizumab Plus Ociperlimab

Arm description:

Participants received 200 mg tislelizumab and 900 mg ociperlimab intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.

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

Dosage and administration details:

200 mg administered intravenously once every 3 weeks

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

Dosage and administration details:

900 mg administered intravenously once every 3 weeks

Arm title	Arm B: Tislelizumab Plus Placebo
------------------	----------------------------------

Arm description:

Participants received 200 mg tislelizumab and placebo intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.

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

Dosage and administration details:

200 mg administered intravenously once every 3 weeks

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously once every 3 weeks

Number of subjects in period 1	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo
Started	62	63
Received Treatment	62	63
Completed	0	0
Not completed	62	63
Study Closed by Sponsor	20	15
Consent withdrawn by subject	2	7
Death	39	36
Lost to follow-up	1	5

Baseline characteristics

Reporting groups

Reporting group title	Arm A: Tislelizumab Plus Ociperlimab
Reporting group description:	
Participants received 200 mg tislelizumab and 900 mg ociperlimab intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.	
Reporting group title	Arm B: Tislelizumab Plus Placebo
Reporting group description:	
Participants received 200 mg tislelizumab and placebo intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.	

Reporting group values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo	Total
Number of subjects	62	63	125
Age categorical			
Units: Subjects			
Between 18 and 65 years	40	27	67
>=65 years	22	36	58
Age continuous			
Units: years			
arithmetic mean	61.4	63.6	-
standard deviation	± 7.31	± 7.33	-
Gender categorical			
Units: Subjects			
Female	4	10	14
Male	58	53	111
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	56	54	110
White	3	5	8
Not Reported	3	3	6
Eastern Cooperative Oncology Group Performance Status (ECOG PS)			
ECOG Performance Status is used to assess a patient's disease status, and how the disease affects daily living activities according to the following scale: 0 = Fully active, able to carry out all activities without restriction; 1= Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2= Ambulatory and capable of all self-care, unable to carry out any work activities. Up and about > 50% of waking hours; 3= Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4= Completely disabled, confined to bed or chair.			
Units: Subjects			
0 (Fully active)	16	15	31
1 (Restricted but ambulatory)	46	48	94
Number of Organs With Metastases			
Units: Subjects			
≤ 1 organ	32	33	65
≥ 2 organs	30	30	60
Region			

Units: Subjects			
Asia	54	54	108
Non-Asia	8	9	17

End points

End points reporting groups

Reporting group title	Arm A: Tislelizumab Plus Ociperlimab
Reporting group description: Participants received 200 mg tislelizumab and 900 mg ociperlimab intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.	
Reporting group title	Arm B: Tislelizumab Plus Placebo
Reporting group description: Participants received 200 mg tislelizumab and placebo intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.	

Primary: Objective Response Rate (ORR) Assessed by the Investigator

End point title	Objective Response Rate (ORR) Assessed by the Investigator
End point description: ORR is defined as the percentage of participants with a best overall response of confirmed complete response (CR) or partial response (PR) assessed by the Investigator per the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Response evaluations were performed using computed tomography or magnetic resonance imaging (MRI) approximately every 6 weeks for the first 54 weeks and every 12 weeks thereafter. CR: Disappearance of all target and non-target lesions; any pathological lymph nodes (whether target or non-target) < 10 mm, and no new lesions. PR: At least 30% decrease in the size of target lesions, no progression of non-target lesions and no new lesions, or disappearance of target lesions with persistence of ≥ 1 non-target lesion(s) and/or maintenance of tumor marker level above the normal limits and no new lesions. CR/PR must have been confirmed ≥ 4 weeks after response was first observed. The Intent-to-Treat (ITT) Analysis Set included all randomized participants.	
End point type	Primary
End point timeframe: Up to the primary analysis data cutoff date of 01 February 2023; median (range) time on follow-up was 7.4 (0.5 - 20.1) months in Arm A and 6.4 (0.4 - 20.2) months in Arm B.	

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: percentage of participants				
number (confidence interval 95%)	30.6 (19.6 to 43.7)	20.6 (11.5 to 32.7)		

Statistical analyses

Statistical analysis title	Primary Analysis of ORR
Statistical analysis description: A Mantel-Haenszel common risk difference stratified by the stratification factors (ECOG PS score [0 vs 1] and number of organs with metastases [≤ 1 vs ≥ 2]) was estimated, along with its 95% confidence	

interval constructed by a normal approximation and Sato's variance estimator.

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.2114 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Stratified Risk Difference
Point estimate	9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	25.3

Notes:

[1] - The primary endpoint ORR was tested at a 2-sided alpha of 0.05.

[2] - Cochran-Mantel-Haenszel method stratified by the stratification factors (ECOG PS score [0 vs 1] and number of organs with metastases [≤ 1 vs ≥ 2]).

Secondary: Overall Survival

End point title	Overall Survival
-----------------	------------------

End point description:

Overall survival (OS) is defined as the time from the date of randomization until the date of death due to any cause.

Median overall survival was estimated using the Kaplan-Meier method. For participants who were still alive at the end of the trial, OS was censored at the last known alive date or the date of data cutoff, whichever was earlier.

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization to the end of the study, median (range) time on follow-up was 10.0 (0.5 - 29.9) months in Arm A and 7.8 (0.4 - 29.3) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: months				
median (confidence interval 95%)	10.2 (7.9 to 19.5)	9.3 (6.4 to 14.8)		

Statistical analyses

Statistical analysis title	Analysis of OS
----------------------------	----------------

Statistical analysis description:

Hazard ratio and 95% confidence intervals (CIs) were estimated using a Cox regression model stratified by the selected stratification factors (ECOG PS score [0 vs 1] and the number of organs with metastases [≤ 1 vs ≥ 2]).

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab
-------------------	--

	Plus Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.45

Secondary: Objective Response Rate Assessed by the Independent Review Committee

End point title	Objective Response Rate Assessed by the Independent Review Committee
-----------------	--

End point description:

ORR is defined as the percentage of participants who had a best overall response of confirmed complete response (CR) or partial response (PR) assessed by the Independent Review Committee (IRC) according to RECIST v1.1.

Response evaluations were performed using computed tomography or MRI approximately every 6 weeks for the first 54 weeks and then every 12 weeks thereafter.

CR: Disappearance of all target and non-target lesions; any pathological lymph nodes (whether target or non-target) < 10 mm, and no new lesions.

PR: At least a 30% decrease in the size of target lesions, with no progression of non-target lesions and no new lesions, or disappearance of target lesions with persistence of 1 or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits, and no new lesions.

Response (CR or PR) must have been confirmed 4 weeks or later after the first response was observed.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to the primary analysis data cutoff date of 01 February 2023; median (range) time on follow-up was 7.4 (0.5 - 20.1) months in Arm A and 6.4 (0.4 - 20.2) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: percentage of participants				
number (confidence interval 95%)	32.3 (20.9 to 45.3)	25.4 (15.3 to 37.9)		

Statistical analyses

Statistical analysis title	Analysis of ORR per IRC
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Stratified Risk Difference
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	22.5

Secondary: Progression-free Survival (PFS) Assessed by the Independent Review Committee

End point title	Progression-free Survival (PFS) Assessed by the Independent Review Committee
-----------------	--

End point description:

Progression-free survival is defined as the time from the date of randomization to the date of first documentation of progressive disease assessed by the Independent Review Committee per RECIST v1.1, or death, whichever occurred first.

Median PFS was estimated using the Kaplan-Meier method.

Progressive Disease (PD): At least a 20% increase in the size of target lesions with an absolute increase of at least 5 mm, or unequivocal progression of existing non-target lesions, or the appearance of any new lesions.

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization up to the primary analysis data cutoff date of 01 February 2023; median (range) time on follow-up was 7.4 (0.5 - 20.1) months in Arm A and 6.4 (0.4 - 20.2) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: months				
median (confidence interval 95%)	3.6 (2.7 to 5.1)	2.8 (1.9 to 6.9)		

Statistical analyses

Statistical analysis title	Analysis of PFS per IRC
----------------------------	-------------------------

Statistical analysis description:

Hazard ratio and 95% CIs were estimated using a Cox regression model stratified by the selected stratification factors (ECOG PS score [0 vs 1] and the number of organs with metastases [≤ 1 vs ≥ 2]).

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
-------------------	---

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.59

Secondary: Progression-free Survival (PFS) Assessed by the Investigator

End point title	Progression-free Survival (PFS) Assessed by the Investigator
End point description:	
<p>Progression-free survival is defined as the time from the date of randomization to the date of first documentation of progressive disease assessed by the Investigator per RECIST v1.1, or death, whichever occurred first.</p> <p>Median PFS was estimated using the Kaplan-Meier method.</p> <p>Progressive Disease (PD): At least a 20% increase in the size of target lesions with an absolute increase of at least 5 mm, or unequivocal progression of existing non-target lesions, or the appearance of any new lesions.</p>	
End point type	Secondary
End point timeframe:	
<p>From randomization to the end of the study, median (range) time on follow-up was 10.0 (0.5 - 29.9) months in Arm A and 7.8 (0.4 - 29.3) months in Arm B.</p>	

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: months				
median (confidence interval 95%)	3.4 (1.8 to 5.1)	3.4 (1.9 to 4.1)		

Statistical analyses

Statistical analysis title	Analysis of OS by Investigator
Statistical analysis description:	
<p>Hazard ratio and 95% CIs were estimated using a Cox regression model stratified by the selected stratification factors (ECOG PS score [0 vs 1] and the number of organs with metastases [≤ 1 vs ≥ 2]).</p>	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.61

Secondary: Duration Of Response (DOR) Assessed by the Independent Review Committee

End point title	Duration Of Response (DOR) Assessed by the Independent Review Committee
-----------------	---

End point description:

Duration of response is defined as the time from the first determination of an objective response (CR or PR) until the first documentation of progressive disease as assessed by the Independent Review Committee per RECIST v1.1, or death, whichever occurred first.

Median DOR was estimated using the Kaplan-Meier method. The analysis includes participants in the Intent-to-Treat Analysis Set who had an objective response per IRC assessment. "99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization up to the primary analysis data cutoff date of 01 February 2023; median (range) time on follow-up was 7.4 (0.5 - 20.1) months in Arm A and 6.4 (0.4 - 20.2) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	16		
Units: months				
median (confidence interval 95%)	14.6 (7.2 to 99999)	99999 (4.2 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration Of Response (DOR) Assessed by the Investigator

End point title	Duration Of Response (DOR) Assessed by the Investigator
-----------------	---

End point description:

Duration of response is defined as the time from the first determination of an objective response (CR or PR) until the first documentation of progressive disease as assessed by the Investigator per RECIST v1.1, or death, whichever occurred first.

Median DOR was estimated using the Kaplan-Meier method. The analysis includes participants in the

Intent-to-Treat Analysis Set who had an objective response per Investigator assessment. "99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization to the end of the study, median (range) time on follow-up was 10.0 (0.5 - 29.9) months in Arm A and 7.8 (0.4 - 29.3) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	14		
Units: months				
median (confidence interval 95%)	11.3 (5.7 to 99999)	99999 (4.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate Assessed by the IRC And the Investigator

End point title	Disease Control Rate Assessed by the IRC And the Investigator
-----------------	---

End point description:

Disease Control Rate is defined as the percentage of participants who had confirmed CR, PR, or stable disease (SD) assessed by the IRC and the investigator per RECIST v1.1. Response evaluations were performed using computed tomography or MRI approximately every 6 weeks for the first 54 weeks and then every 12 weeks thereafter.

CR: Disappearance of all target and non-target lesions; any pathological lymph nodes (whether target or non-target) < 10 mm, and no new lesions.

PR: At least a 30% decrease in the size of target lesions, with no progression of non-target lesions and no new lesions, or disappearance of target lesions with persistence of 1 or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits, and no new lesions.

SD: Neither sufficient shrinkage in size of lesions to qualify for PR nor sufficient increase to qualify for PD, and no new lesions.

Response (CR or PR) must have been confirmed 4 weeks or later after the first response.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to the primary analysis data cutoff date of 01 February 2023; median (range) time on follow-up was 7.4 (0.5 - 20.1) months in Arm A and 6.4 (0.4 - 20.2) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: Percentage of participants				
number (confidence interval 95%)				

Investigator assessment	61.3 (48.1 to 73.4)	58.7 (45.6 to 71.0)		
Independent Review Committee	64.5 (51.3 to 76.3)	58.7 (45.6 to 71.0)		

Statistical analyses

Statistical analysis title	Analysis of DCR Assessed by the Investigator
Statistical analysis description:	
Mantel-Haenszel common risk difference stratified by the stratification factors (ECOG PS score [0 vs 1] and number of organs with metastases [≤ 1 vs ≥ 2]).	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Stratified Risk Difference
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	19.9

Statistical analysis title	Analysis of DCR Assessed by the IRC
Statistical analysis description:	
Mantel-Haenszel common risk difference stratified by the stratification factors (ECOG PS score [0 vs 1] and number of organs with metastases [≤ 1 vs ≥ 2]).	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Stratified Risk Difference
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	21.8

Secondary: Clinical Benefit Rate Assessed by the IRC and the Investigator

End point title	Clinical Benefit Rate Assessed by the IRC and the Investigator
-----------------	--

End point description:

Clinical benefit rate is defined as the percentage of participants who achieved a confirmed complete response, partial response, or durable stable disease assessed by the IRC and the Investigator per RECIST v1.1. Response evaluations were performed using computed tomography or MRI approximately

every 6 weeks for the first 54 weeks and then every 12 weeks thereafter.

CR: Disappearance of all target and non-target lesions; any pathological lymph nodes (whether target or non-target) < 10 mm, and no new lesions.

PR: At least a 30% decrease in the size of target lesions, with no progression of non-target lesions and no new lesions, or disappearance of target lesions with persistence of 1 or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits, and no new lesions.

Durable SD: Stable disease for ≥ 24 weeks. Response (CR or PR) must have been confirmed 4 weeks or later after the first response.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to the primary analysis data cutoff date of 01 February 2023; median (range) time on follow-up was 7.4 (0.5 - 20.1) months in Arm A and 6.4 (0.4 - 20.2) months in Arm B.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: percentage of participants				
number (confidence interval 95%)				
Investigator Assessment	33.9 (22.3 to 47.0)	30.2 (19.2 to 43.0)		
Independent Review Committee	32.3 (20.9 to 45.3)	27.0 (16.6 to 39.7)		

Statistical analyses

Statistical analysis title	Analysis of CBR Assessed by the Investigator
----------------------------	--

Statistical analysis description:

Mantel-Haenszel common risk difference stratified by the stratification factors (ECOG PS score [0 vs 1] and number of organs with metastases [≤ 1 vs ≥ 2]).

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Stratified Risk Difference
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.7
upper limit	20.4

Statistical analysis title	Analysis of CBR Assessed by the IRC
----------------------------	-------------------------------------

Statistical analysis description:

Mantel-Haenszel common risk difference stratified by the stratification factors (ECOG PS score [0 vs 1] and number of organs with metastases [≤ 1 vs ≥ 2]).

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Stratified Risk Difference
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	21

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

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

End point description:

The EORTC QLQ-30 contains 30 questions that incorporate 5 functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning), 1 global health status scale, 3 symptom scales (fatigue, nausea and vomiting, and pain), and 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The participant answers questions about their health during the past week. There are 28 questions answered on a 4-point scale where 1 = Not at all (best) and 4 = Very Much (worst) and 2 global health quality of life (QOL) questions answered on a 7-point scale where 1 = Very poor and 7 = Excellent. Raw scores are transformed into a 0 to 100 scale via linear transformation. Higher scores in GHS and functional scales indicate better quality of life.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Cycle 5 Day 1 and Cycle 7 Day 1 (each cycle was 3 weeks)

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50 ^[3]	48 ^[4]		
Units: score on a scale				
least squares mean (confidence interval 95%)				
Global Health Status/QOL: Cycle 5	1.7 (-5.6 to 8.9)	-0.1 (-7.5 to 7.4)		
Global Health Status/QOL: Cycle 7	0.3 (-5.6 to 6.1)	-2.8 (-8.8 to 3.2)		
Physical Functioning: Cycle 5	-0.5 (-4.3 to 3.3)	1.2 (-2.8 to 5.2)		
Physical Functioning: Cycle 7	-4.4 (-11.2 to 2.5)	-3.9 (-11.0 to 3.3)		

Notes:

[3] - ITT Analysis Set with EORTC QLQ-C30 Baseline values;

Cycle 5: n=32;

Cycle 7: n=21

[4] - ITT Analysis Set with EORTC QLQ-C30 Baseline values;

Cycle 5: n=30;

Cycle 7: n=20

Statistical analyses

Statistical analysis title	Analysis of GHS/QoL at Cycle 5
Statistical analysis description:	
The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	11.9

Statistical analysis title	Analysis of GHS/QoL at Cycle 7
Statistical analysis description:	
The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	11.2

Statistical analysis title	Analysis of Physical Functioning at Cycle 5
Statistical analysis description:	
The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and	

visit as a repeated measure, with an unstructured covariance structure.

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	3.7

Statistical analysis title	Analysis of Physical Functioning at Cycle 7
Statistical analysis description:	
The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.3
upper limit	9.3

Secondary: Change From Baseline in EORTC Quality of Life Oesophageal Cancer Questionnaires 18 (QLQ-OES18) Dysphagia, Eating, Reflux and Pain Scales

End point title	Change From Baseline in EORTC Quality of Life Oesophageal Cancer Questionnaires 18 (QLQ-OES18) Dysphagia, Eating, Reflux and Pain Scales
End point description:	
The EORTC-QLQ-OES18 is the specific esophageal symptoms module of the QLQ-C30. QLQ-OES18 is comprised of 18 questions grouped into 4 multi-item subscales: Dysphagia (3 items), Eating (4 items), Reflux (2 items), and Pain (3 items) and 6 single item subscales (saliva swallowing, choking, dry mouth, taste, coughing, and talking). Participants indicate the extent to which they have experienced symptoms on a scale from 1 (Not at all) to 4 (Very much). Scores are calculated and transformed to a scale from 0 to 100; higher scores indicate a higher level of symptomatology or problems.	
End point type	Secondary
End point timeframe:	
Baseline, Cycle 5 Day 1 and Cycle 7 Day 1 (each cycle was 3 weeks)	

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[5]	48 ^[6]		
Units: score on a scale				
least squares mean (confidence interval 95%)				
Dysphagia: Cycle 5	-5.9 (-14.2 to 2.4)	4.1 (-4.7 to 12.8)		
Dysphagia: Cycle 7	-3.5 (-15.4 to 8.5)	7.3 (-5.2 to 19.8)		
Eating: Cycle 5	-1.6 (-6.6 to 3.3)	-1.3 (-6.6 to 4.1)		
Eating: Cycle 7	-2.8 (-9.1 to 3.6)	6.6 (-0.2 to 13.4)		
Reflux: Cycle 5	1.9 (-4.6 to 8.3)	-0.4 (-7.1 to 6.4)		
Reflux: Cycle 7	2.7 (-4.8 to 10.1)	4.0 (-3.8 to 11.8)		
Pain: Cycle 5	0.1 (-5.5 to 5.6)	-0.7 (-6.5 to 5.1)		
Pain: Cycle 7	-2.1 (-7.1 to 3.0)	3.3 (-2.0 to 8.5)		

Notes:

[5] - ITT Analysis Set with QLQ-OES18 Baseline values;
Cycle 5 n=34 (33 for Reflux & Pain);
Cycle 7 n=22

[6] - ITT Analysis Set with QLQ-OES18 Baseline values;
Cycle 5 n=30 (29 for Eating);
Cycle 7 n=20

Statistical analyses

Statistical analysis title	Analysis of Dysphagia at Cycle 5
Statistical analysis description:	
The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.5
upper limit	1.6

Statistical analysis title	Analysis of Dysphagia at Cycle 7
Statistical analysis description: The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.8
upper limit	6.3

Statistical analysis title	Analysis of Eating at Cycle 5
Statistical analysis description: The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	6.6

Statistical analysis title	Analysis of Eating at Cycle 7
Statistical analysis description: The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.5
upper limit	-0.3

Statistical analysis title	Analysis of Reflux at Cycle 5
-----------------------------------	-------------------------------

Statistical analysis description:

The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	11.2

Statistical analysis title	Analysis of Reflux at Cycle 7
-----------------------------------	-------------------------------

Statistical analysis description:

The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.

Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	9

Statistical analysis title	Analysis of Pain at Cycle 5
Statistical analysis description: The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	8.5

Statistical analysis title	Analysis of Pain at Cycle 7
Statistical analysis description: The mixed effect model analysis included the questionnaire score as dependent variable; baseline score, stratification factors, treatment arm, visit, and treatment arm by visit interaction as fixed effects; and visit as a repeated measure, with an unstructured covariance structure.	
Comparison groups	Arm A: Tislelizumab Plus Ociperlimab v Arm B: Tislelizumab Plus Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	1.7

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)
-----------------	---

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study drugs, whether related to study drugs or not.

An SAE is any event that:

-Resulted in death.

- Was life-threatening.
- Required hospitalization or prolongation of existing hospitalization.
- Resulted in disability/incapacity.
- Was a congenital anomaly/birth defect.
- Was considered a significant medical AE by the Investigator.

AEs were considered related to study drug if there was evidence to suggest a causal relationship. The investigator assessed the severity of each AE reported based on National Cancer Institute-Common Terminology Criteria for AEs (NCI-CTCAE) v5.0, where ≥ 3 includes severe or medically significant, life-threatening events or death related to AE. Immune-mediated AEs were diagnosed by the investigator. TEAEs leading to death excludes death due to disease under study.

End point type	Secondary
----------------	-----------

End point timeframe:

From first dose of study drug until 30 days after last dose; median duration of treatment was 3.45 months in Tislelizumab + Ociperlimab arm and 2.79 months in the Tislelizumab + Placebo arm.

End point values	Arm A: Tislelizumab Plus Ociperlimab	Arm B: Tislelizumab Plus Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	63		
Units: participants				
Any TEAEs	58	60		
TEAE \geq Grade 3	28	28		
Serious AEs	27	28		
Related SAEs	13	13		
TEAEs Leading to Treatment Discontinuation	9	10		
TEAEs Leading to Death	4	4		
Any Immune-Mediated AE	31	21		
Immune-Mediated AE \geq Grade 3	8	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs are reported from first dose of study drug until 30 days after last dose; median duration of treatment was 3.45 months in Tislelizumab + Ociperlimab arm and 2.79 months in the Tislelizumab + Placebo arm.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Arm B: Tislelizumab Plus Placebo
-----------------------	----------------------------------

Reporting group description:

Participants received 200 mg tislelizumab plus placebo intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.

Reporting group title	Arm A: Tislelizumab Plus Ociperlimab
-----------------------	--------------------------------------

Reporting group description:

Participants received 200 mg tislelizumab plus 900 mg ociperlimab intravenously once every 3 weeks until disease progression, unacceptable toxicity, or withdrawal of informed consent, whichever occurred first.

Serious adverse events	Arm B: Tislelizumab Plus Placebo	Arm A: Tislelizumab Plus Ociperlimab	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 63 (44.44%)	27 / 62 (43.55%)	
number of deaths (all causes)	36	39	
number of deaths resulting from adverse events	10	8	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 63 (1.59%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 2	
General physical health deterioration			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			

Benign prostatic hyperplasia subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary oedema			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Productive cough			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 63 (1.59%)	4 / 62 (6.45%)	
occurrences causally related to treatment / all	0 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fracture			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			

subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated myocarditis			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Dysphagia			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal obstruction			
subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vomiting			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Immune-mediated dermatitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Herpes zoster			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 63 (7.94%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	5 / 5	1 / 2	
deaths causally related to treatment / all	2 / 2	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Arm B: Tislelizumab Plus Placebo	Arm A: Tislelizumab Plus Ociperlimab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 63 (85.71%)	57 / 62 (91.94%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 63 (1.59%)	4 / 62 (6.45%)	
occurrences (all)	1	4	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 63 (0.00%)	5 / 62 (8.06%)	
occurrences (all)	0	5	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 63 (9.52%)	5 / 62 (8.06%)	
occurrences (all)	8	6	
Chest pain			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Chills			
subjects affected / exposed	0 / 63 (0.00%)	3 / 62 (4.84%)	
occurrences (all)	0	3	
Fatigue			
subjects affected / exposed	5 / 63 (7.94%)	8 / 62 (12.90%)	
occurrences (all)	5	8	
Malaise			
subjects affected / exposed	3 / 63 (4.76%)	1 / 62 (1.61%)	
occurrences (all)	3	1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences (all)	2	3	
Oedema peripheral			
subjects affected / exposed	1 / 63 (1.59%)	2 / 62 (3.23%)	
occurrences (all)	1	2	
Peripheral swelling			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences (all)	2	0	

Pyrexia subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 5	4 / 62 (6.45%) 6	
Respiratory, thoracic and mediastinal disorders Pleural effusion subjects affected / exposed occurrences (all)	3 / 63 (4.76%) 3	3 / 62 (4.84%) 4	
Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 63 (4.76%) 3	0 / 62 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	3 / 63 (4.76%) 3	5 / 62 (8.06%) 5	
Dysphonia subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	1 / 62 (1.61%) 1	
Cough subjects affected / exposed occurrences (all)	13 / 63 (20.63%) 17	7 / 62 (11.29%) 7	
Productive cough subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 4	4 / 62 (6.45%) 4	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 6	4 / 62 (6.45%) 6	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	9 / 63 (14.29%) 9	4 / 62 (6.45%) 7	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	8 / 63 (12.70%) 8	4 / 62 (6.45%) 9	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	1 / 62 (1.61%) 1	

Blood bilirubin increased			
subjects affected / exposed	3 / 63 (4.76%)	0 / 62 (0.00%)	
occurrences (all)	3	0	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)	
occurrences (all)	3	3	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 63 (1.59%)	5 / 62 (8.06%)	
occurrences (all)	2	7	
Blood creatinine increased			
subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences (all)	2	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)	
occurrences (all)	1	4	
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences (all)	2	0	
Blood urea increased			
subjects affected / exposed	3 / 63 (4.76%)	1 / 62 (1.61%)	
occurrences (all)	3	1	
Electrocardiogram high voltage			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Lymphocyte count decreased			
subjects affected / exposed	3 / 63 (4.76%)	6 / 62 (9.68%)	
occurrences (all)	3	9	
Neutrophil count decreased			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	10	5	
Platelet count decreased			
subjects affected / exposed	3 / 63 (4.76%)	2 / 62 (3.23%)	
occurrences (all)	3	2	
SARS-CoV-2 test positive			

subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	0 / 62 (0.00%) 0	
Tri-iodothyronine decreased subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	0 / 62 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	6 / 63 (9.52%) 6	10 / 62 (16.13%) 11	
White blood cell count decreased subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 10	4 / 62 (6.45%) 9	
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	2 / 62 (3.23%) 2	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	4 / 62 (6.45%) 4	
Headache subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	4 / 62 (6.45%) 4	
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	2 / 62 (3.23%) 2	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	20 / 63 (31.75%) 25	17 / 62 (27.42%) 29	
Thrombocytopenia subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 5	1 / 62 (1.61%) 1	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	2 / 62 (3.23%) 2	
Abdominal pain upper			

subjects affected / exposed	3 / 63 (4.76%)	2 / 62 (3.23%)	
occurrences (all)	5	2	
Constipation			
subjects affected / exposed	8 / 63 (12.70%)	13 / 62 (20.97%)	
occurrences (all)	8	14	
Diarrhoea			
subjects affected / exposed	6 / 63 (9.52%)	9 / 62 (14.52%)	
occurrences (all)	6	9	
Dry mouth			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Dysphagia			
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)	
occurrences (all)	5	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 63 (3.17%)	4 / 62 (6.45%)	
occurrences (all)	2	5	
Haemorrhoids			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	5 / 63 (7.94%)	4 / 62 (6.45%)	
occurrences (all)	5	4	
Oesophageal obstruction			
subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)	
occurrences (all)	1	3	
Stomatitis			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	5 / 63 (7.94%)	5 / 62 (8.06%)	
occurrences (all)	5	5	
Skin and subcutaneous tissue disorders			

Dermatitis subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all)	1 / 63 (1.59%)	3 / 62 (4.84%)	
	1	4	
	3 / 63 (4.76%)	8 / 62 (12.90%)	
	3	9	
	2 / 63 (3.17%)	6 / 62 (9.68%)	
	2	6	
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	0 / 63 (0.00%)	2 / 62 (3.23%)	
	0	2	
	0 / 63 (0.00%)	3 / 62 (4.84%)	
	0	3	
	13 / 63 (20.63%)	11 / 62 (17.74%)	
	15	14	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Pain in extremity	0 / 63 (0.00%)	3 / 62 (4.84%)	
	0	4	
	6 / 63 (9.52%)	3 / 62 (4.84%)	
	6	4	
	1 / 63 (1.59%)	2 / 62 (3.23%)	
	1	2	
	2 / 63 (3.17%)	1 / 62 (1.61%)	
	2	1	

subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	2 / 62 (3.23%) 2	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 63 (3.17%)	6 / 62 (9.68%)	
occurrences (all)	3	7	
Pneumonia			
subjects affected / exposed	4 / 63 (6.35%)	3 / 62 (4.84%)	
occurrences (all)	4	3	
Tuberculosis			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	6 / 63 (9.52%)	2 / 62 (3.23%)	
occurrences (all)	7	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 63 (17.46%)	6 / 62 (9.68%)	
occurrences (all)	12	6	
Hypercalcaemia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Hyperchloraemia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Hyperglycaemia			
subjects affected / exposed	2 / 63 (3.17%)	3 / 62 (4.84%)	
occurrences (all)	2	3	
Hyperkalaemia			
subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)	
occurrences (all)	3	9	
Hypernatraemia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	
occurrences (all)	0	2	
Hyperuricaemia			

subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)
occurrences (all)	1	3
Hypoalbuminaemia		
subjects affected / exposed	10 / 63 (15.87%)	9 / 62 (14.52%)
occurrences (all)	17	14
Hypocalcaemia		
subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)
occurrences (all)	1	3
Hypochloraemia		
subjects affected / exposed	4 / 63 (6.35%)	3 / 62 (4.84%)
occurrences (all)	5	3
Hypokalaemia		
subjects affected / exposed	6 / 63 (9.52%)	8 / 62 (12.90%)
occurrences (all)	6	8
Hypomagnesaemia		
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)
occurrences (all)	2	2
Hyponatraemia		
subjects affected / exposed	7 / 63 (11.11%)	9 / 62 (14.52%)
occurrences (all)	8	10
Hypophosphataemia		
subjects affected / exposed	0 / 63 (0.00%)	3 / 62 (4.84%)
occurrences (all)	0	4
Hypoproteinaemia		
subjects affected / exposed	1 / 63 (1.59%)	2 / 62 (3.23%)
occurrences (all)	1	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2022	Protocol Amendment 1.0 Key Changes: <ul style="list-style-type: none">• Revised the expected number of randomized patients from approximately 280 to approximately 120, as a result of the wide use of anti-PD-L1 agents in earlier lines of therapy and consequent enrollment difficulties. The patient enrollment was incomplete by the release of Protocol Amendment 1.0.• Converted OS from a primary to secondary objective because the reduced sample size would not support OS as a primary endpoint.• Updated the study design to unblind the sponsor (the sponsor was unblinded but investigators, site staff, and patients remained blinded) to allow the sponsor to review data across treatment arms.
27 February 2023	Protocol Amendment 2.0 Key Changes: <ul style="list-style-type: none">• Deleted the GLP compliance sentence from the pivotal toxicology studies based on the latest Tislelizumab Investigator's Brochure.• Added the patient supply treatment program to clarify the opportunity for continued treatment according to the current practice of the sponsor.• Revised the testing method of the null hypothesis of ORR from the Miettinen and Nurminen test to Cochran-Mantel-Haenszel method, as the latter one is a more commonly used testing method for ORR.• Revised the percentage and number of the OS events from 70% (84 deaths) of the total sample size of 120 patients to 60% (72 deaths) in the secondary efficacy analysis as a sponsor's decision to change data maturity for OS analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported