Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Clinical Study Comparing the Efficacy and Safety of Tislelizumab (BGB-A317) plus Platinum and Fluoropyrimidine Versus Placebo plus Platinum and Fluoropyrimidine as First-Line Treatment in Patients with Locally Advanced Unresectable or Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma

Summary

EudraCT number	2018-000312-24
Trial protocol	PL ES GB FR IT RO
Global end of trial date	27 August 2024

Results information

Result version number	v1 (current)
This version publication date	16 May 2025
First version publication date	16 May 2025

Trial information

Trial identification

Sponsor protocol code	BGB-A317-305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03777657
WHO universal trial number (UTN)	-
Other trial identifiers	ChinaDrugTrials: CTR20181841

Notes:

Sponsors

Sponsor organisation name	BeiGene
Sponsor organisation address	1840 Gateway Drive, San Mateo, United States, 94404
Public contact	BeiGene Clinical Support, BeiGene USA, Inc., 1 877-828-5568, clinicaltrials@beigene.com
Scientific contact	BeiGene Clinical Support, BeiGene USA, Inc., 1 877-828-5568, clinicaltrials@beigene.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was designed to compare the efficacy and safety of tislelizumab plus chemotherapy versus placebo plus chemotherapy as the first treatment (first-line) for adults diagnosed with locally advanced unresectable or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Protection of trial subjects:

This study was conducted in accordance with 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, any 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 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	China: 499
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	Japan: 101
Country: Number of subjects enrolled	Korea, Republic of: 131
Country: Number of subjects enrolled	Russian Federation: 98
Country: Number of subjects enrolled	Türkiye: 17
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Italy: 18
Worldwide total number of subjects	997
EEA total number of subjects	101

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)	653
From 65 to 84 years	342
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 141 study centers across Asia, Europe, and North America. Adults with histologically confirmed, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma and no previous systemic therapy for advanced disease were recruited.

Pre-assignment

Screening details:

Participants were randomly assigned to one of two treatment groups. Randomization was stratified according to region, programmed cell death protein ligand-1 (PD-L1) expression, peritoneal metastases, and investigator's choice of chemotherapy.

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	Tislelizumab + Chemotherapy

Arm description:

Participants received 200 mg of tislelizumab intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Chemotherapy consisted of 1000 mg/m² capecitabine twice daily on Days 1-14 and 130 mg/m² oxaliplatin on Day 1, or 800 mg/m² 5-fluorouracil (5-FU) on Days 1-5 and 80 mg/m² cisplatin on Day 1 of each 21-day cycle. Thereafter, participants continued treatment with 200 mg tislelizumab once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.

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:

Tislelizumab 200 mg administered by intravenous infusion on Day 1 of each 21-day cycle.

Investigational medicinal product name	Chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Chemotherapy consisted of 1000 mg/m² capecitabine orally twice daily on Days 1-14 and 130 mg/m² oxaliplatin IV on Day 1 of each 21-day cycle, or 800 mg/m² 5-fluorouracil (5-FU) continuous IV on Days 1-5 and 80 mg/m² cisplatin IV on Day 1 of each 21-day cycle.

Arm title	Placebo + Chemotherapy

Arm description:

Participants received placebo intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Chemotherapy consisted of 1000 mg/m² capecitabine twice daily on Days 1-14 and 130 mg/m² oxaliplatin on Day 1, or 800 mg/m² 5-FU on Days 1-5 and 80 mg/m² cisplatin on Day 1 of each 21-day cycle. Thereafter, participants continued treatment with placebo once

every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.

Arm type	Active comparator
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:

Placebo to tislelizumab administered by intravenous infusion on Day 1 of each 21-day cycle.

Investigational medicinal product name	Chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Chemotherapy consisted of 1000 mg/m² capecitabine orally twice daily on Days 1-14 and 130 mg/m² oxaliplatin IV on Day 1 of each 21-day cycle, or 800 mg/m² 5-fluorouracil (5-FU) continuous IV on Days 1-5 and 80 mg/m² cisplatin IV on Day 1 of each 21-day cycle.

Number of subjects in period 1	Tislelizumab + Chemotherapy	Placebo + Chemotherapy
Started	501	496
Received Treatment	498	494
Completed	1	0
Not completed	500	496
Study Closed by Sponsor	77	38
Consent withdrawn by subject	20	17
Death	397	431
Lost to follow-up	6	10

Baseline characteristics

Reporting groups	
Reporting group title	Tislelizumab + Chemotherapy
Reporting group description:	
Participants received 200 mg of tislelizumab intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Chemotherapy consisted of 1000 mg/m² capecitabine twice daily on Days 1-14 and 130 mg/m² oxaliplatin on Day 1, or 800 mg/m² 5-fluorouracil (5-FU) on Days 1-5 and 80 mg/m² cisplatin on Day 1 of each 21-day cycle. Thereafter, participants continued treatment with 200 mg tislelizumab once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.	
Reporting group title	Placebo + Chemotherapy
Reporting group description:	
Participants received placebo intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Chemotherapy consisted of 1000 mg/m² capecitabine twice daily on Days 1-14 and 130 mg/m² oxaliplatin on Day 1, or 800 mg/m² 5-FU on Days 1-5 and 80 mg/m² cisplatin on Day 1 of each 21-day cycle. Thereafter, participants continued treatment with placebo once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.	

Reporting group values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy	Total
Number of subjects	501	496	997
Age categorical Units: Subjects			
Between 18 and 65 years	340	313	653
>=65 years	161	183	344
Age continuous Units: years			
arithmetic mean	58.8	59.7	
standard deviation	± 11.07	± 11.20	-
Gender categorical Units: Subjects			
Female	155	150	305
Male	346	346	692
Ethnicity Units: Subjects			
Hispanic or Latino	2	6	8
Not Hispanic or Latino	492	474	966
Unknown or Not Reported	7	16	23
Race Units: Subjects			
Asian	376	372	748
White	116	107	223
Not Reported	8	16	24
Other	1	0	1
Unknown	0	1	1
Geographic Region Units: Subjects			
China (including Taiwan)	259	257	516
Japan and South Korea	117	115	232

North America/Europe	125	124	249
Primary Tumor Location			
*One participant in the placebo + chemotherapy arm did not report primary location and disease stage, as the diagnosis of this participant was updated from gastric adenocarcinoma to be pancreatic cancer after randomization.			
Units: Subjects			
Stomach	405	395	800
Gastro-oesophageal junction	96	100	196
Other*	0	1	1
PD-L1 Expression			
PDL1 expression was assessed by a central laboratory using the TAP score, defined as total percentage of tumor area (tumor and any desmoplastic stroma) covered by tumor cells with PD-L1 membrane staining (any intensity), and tumor associated immune cells with PD-L1 staining (any intensity), visually estimated by pathologists using an investigational use only version of the Ventana PDL1 (SP263) assay.			
Units: Subjects			
< 5%	227	224	451
≥ 5%	274	272	546
Presence of Peritoneal Metastasis Units: Subjects			
Yes	220	214	434
No	281	282	563
Investigator Chosen Chemotherapy Units: Subjects			
Oxaliplatin + Capecitabine	466	465	931
Cisplatin + 5-Fluorouracil	35	31	66

End points

End points reporting groups

Reporting group title	Tislelizumab + Chemotherapy

Reporting group description:

Participants received 200 mg of tislelizumab intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Chemotherapy consisted of 1000 mg/m² capecitabine twice daily on Days 1-14 and 130 mg/m² oxaliplatin on Day 1, or 800 mg/m² 5-fluorouracil (5-FU) on Days 1-5 and 80 mg/m² cisplatin on Day 1 of each 21-day cycle. Thereafter, participants continued treatment with 200 mg tislelizumab once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.

Reporting group title	Placebo + Chemotherapy

Reporting group description:

Participants received placebo intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Chemotherapy consisted of 1000 mg/m² capecitabine twice daily on Days 1-14 and 130 mg/m² oxaliplatin on Day 1, or 800 mg/m² 5-FU on Days 1-5 and 80 mg/m² cisplatin on Day 1 of each 21-day cycle. Thereafter, participants continued treatment with placebo once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.

Primary: Overall Survival in PD-L1 Positive Participants

End point title	Overall Survival in PD-L1 Positive Participants

End point description:

Overall survival (OS) is defined as the time from the date of randomization to the date of death due to any cause. Median OS was estimated using the Kaplan-Meier method.
The PD-L1-Positive Analysis Set included all randomized participants whose tumors were PD-L1 positive (defined as PD-L1 TAP score ≥ 5%).

End point type	Primary

End point timeframe:

From randomization up to the primary analysis data cut-off date of 8 October 2021; Median (range) time on follow-up was 11.8 (0.1 - 33.4) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[1]	272[2]		
Units: months				
median (confidence interval 95%)	17.2 (13.9 to 21.3)	12.6 (12.0 to 14.4)		

Notes:

[1] - PD-L1-Positive Analysis Set i

[2] - PD-L1-Positive Analysis Set i

Statistical analyses

Statistical analysis title	Analysis of Overall Survival in PD-L1+ Patients

Statistical analysis description:

The analysis of overall survival was performed using a stratified log-rank test, stratified by region (Asia v Europe/North America) and presence of peritoneal metastasis (yes v no). The stratified overall survival hazard ratio and associated two-sided 95% confidence interval (CI) were estimated using a Cox proportional hazard regression model, including treatment arm as a covariate, and region and presence

of peritoneal metastasis as strata.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	546
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0056 [4]
Method	One-sided Log Rank Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.94

Notes:

[3] - The superiority boundary at the primary overall survival analysis was predefined using the O'Brien-Fleming boundary approximated using the Hwang-Shih-DeCani spending function at 0.0092.
[4] - One-Sided Log-Rank Test stratified by regions (Asia versus Europe/North America) and presence of peritoneal metastasis (yes vs no).

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

End point title	Overall Survival in the Intent-to-Treat (ITT) Analysis Set

End point description:

Overall survival (OS) is defined as the time from the date of randomization to the date of death due to any cause. Median OS was estimated using the Kaplan-Meier method.
The Intent-to-Treat (ITT) Analysis Set included all randomized participants.

End point type	Primary

End point timeframe:

From randomization up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	501	496		
Units: months				
median (confidence interval 95%)	15.0 (13.6 to 16.5)	12.9 (12.1 to 14.1)		

Statistical analyses

Statistical analysis title	Analysis of OS in the ITT Analysis Set

Statistical analysis description:

Analysis of overall survival was performed using a log-rank test, stratified by region (Asia v Europe/North America), PD-L1 expression (PD-L1 TAP score <5% v ≥5%), and presence of peritoneal metastasis (yes v no). The stratified overall survival hazard ratio and 2-sided 95% CI were estimated using a Cox proportional hazard regression model, including treatment arm as a covariate, and using stratification factors region, PD-L1 expression, and presence of peritoneal metastasis as strata.

Comparison groups	Placebo + Chemotherapy v Tislelizumab + Chemotherapy

Number of subjects included in analysis	997
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0011 [6]
Method	One-Sided Log-Rank Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.92

Notes:

[5] - The one sided P value boundary for superiority of overall survival in all randomized participants at final analysis was 0.0226 based on 776 actual observed deaths.
[6] - One-Sided Log-Rank test stratified by region (Asia vs Europe/North America), PD-L1 expression (<5% vs ≥5%), and presence of peritoneal metastasis.

Secondary: Progression-free Survival (PFS) in PD-L1 Positive Participants

End point title	Progression-free Survival (PFS) in PD-L1 Positive Participants

End point description:

Progression-free survival is defined as the time from the date of randomization to the date of the first objectively documented tumor progression assessed by the investigator according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, or death, whichever occurred first.
Median PFS was estimated using the Kaplan-Meier method.

End point type	Secondary

End point timeframe:

From randomization up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[7]	272[8]		
Units: months				
median (confidence interval 95%)	7.2 (5.8 to 8.4)	5.9 (5.6 to 7.0)		

Notes:

[7] - PD-L1 Positive Analysis Set

[8] - PD-L1 Positive Analysis Set

Statistical analyses

Statistical analysis title	Analysis of PFS in PD-L1 Positive Analysis Set

Statistical analysis description:

The stratified hazard ratio and two-sided 95% confidence interval were estimated using a Cox proportional hazard regression model, including treatment arm as a covariate, and region and presence of peritoneal metastasis as strata.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy

Number of subjects included in analysis	546
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.83

Secondary: Overall Response Rate (ORR) in PD-L1 Positive Participants

End point title	Overall Response Rate (ORR) in PD-L1 Positive Participants

End point description:

ORR is defined as the percentage of participants whose best overall response is complete response (CR) or partial response (PR) per Response Evaluation Criteria in Solid Tumors v1.1 assessed by the investigator.
Investigators conducted assessments of radiological tumor response by computed tomography (CT) or magnetic resonance imaging (MRI) per RECIST version 1.1 about every six weeks during the first 48 weeks of the study and every nine weeks thereafter.
CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[9]	272[10]		
Units: percentage of participants				
number (confidence interval 95%)	51.5 (45.4 to 57.5)	42.6 (36.7 to 48.8)		

Notes:

[9] - PD-L1 Positive Analysis Set

[10] - PD-L1 Positive Analysis Set

Statistical analyses

Statistical analysis title	Analysis of ORR in the PD-L1 Positive Analysis Set

Statistical analysis description:

Odds ratio between arms was calculated using the Cochran-Mantel-Haenszel method, stratified by regions (Asia versus Europe/North America) and presence of peritoneal metastasis.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy

Number of subjects included in analysis	546
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.04

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:

Progression-free survival is defined as the time from the date of randomization to the date of the first objectively documented tumor progression assessed by the investigator according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, or death, whichever occurred first.
Median PFS was estimated using the Kaplan-Meier method.

End point type	Secondary

End point timeframe:

From randomization up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	501	496		
Units: months				
median (confidence interval 95%)	6.9 (5.7 to 7.2)	6.2 (5.6 to 6.9)		

Statistical analyses

Statistical analysis title	Analysis of PFS in the ITT Analysis Set

Statistical analysis description:

The stratified hazard ratio and two-sided 95% confidence interval were estimated using a Cox proportional hazard regression model, including treatment arm as a covariate, and region, PD-L1 expression, and presence of peritoneal metastasis as strata.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	997
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.9

Secondary: Overall Response Rate (ORR) in the ITT Analysis Set

End point title	Overall Response Rate (ORR) in the ITT Analysis Set

End point description:

ORR is defined as the percentage of participants whose best overall response is complete response (CR) or partial response (PR) per Response Evaluation Criteria in Solid Tumors v1.1 assessed by the investigator.
Investigators conducted assessments of radiological tumor response by computed tomography (CT) or magnetic resonance imaging (MRI) per RECIST version 1.1 about every six weeks during the first 48 weeks of the study and every nine weeks thereafter.
CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	501	496		
Units: percentage of participants				
number (confidence interval 95%)	47.3 (42.9 to 51.8)	40.5 (36.2 to 45.0)		

Statistical analyses

Statistical analysis title	Analysis of ORR in the ITT Analysis Set

Statistical analysis description:

Odds ratio between arms was calculated using the Cochran-Mantel-Haenszel method, stratified by regions (Asia versus Europe/North America), PD-L1 expression and presence of peritoneal metastasis.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	997
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.72

Secondary: Duration of Response (DOR) in PD-L1 Positive Participants

End point title	Duration of Response (DOR) in PD-L1 Positive Participants

End point description:

DOR is defined as the time from the first determination of an objective response assessed by the investigator per RECIST v1.1, until the first documentation of progression or death, whichever occurred first.
Progressive disease (PD): At least a 20% increase in the size of target lesions, taking as reference the smallest size on study, with an absolute increase of at least 5 mm, unequivocal progression of existing non-target lesions, or any new lesions.
The analysis includes participants in the PD-L1 Positive Analysis Set with an objective response.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141[11]	116[12]		
Units: months				
median (confidence interval 95%)	10.0 (8.2 to 16.8)	6.9 (5.7 to 8.5)		

Notes:

[11] - PD-L1 Positive Analysis Set with an objective response

[12] - PD-L1 Positive Analysis Set with an objective response

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response in the ITT Analysis Set

End point title	Duration of Response in the ITT Analysis Set

End point description:

DOR is defined as the time from the first determination of an objective response assessed by the investigator per RECIST v1.1, until the first documentation of progression or death, whichever occurred first.
Progressive disease (PD): At least a 20% increase in the size of target lesions, taking as reference the smallest size on study, with an absolute increase of at least 5 mm, unequivocal progression of existing non-target lesions, or any new lesions.
The analysis includes participants in the ITT Analysis Set with an objective response.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2

(0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237[13]	201[14]		
Units: months				
median (confidence interval 95%)	8.6 (7.9 to 11.1)	7.2 (6.0 to 8.5)		

Notes:

[13] - Participants with an objective response

[14] - Participants with an objective response

Statistical analyses

No statistical analyses for this end point

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 to a 0 to 100 scale via linear transformation. Higher scores in GHS and functional scales indicate better quality of life.
Participants in the ITT Analysis Set with available data at baseline and each postbaseline visit are included in the analysis.

End point type	Secondary

End point timeframe:

Baseline and Cycle 4 (Week 12) and Cycle 6 (Week 18)

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	465[15]	467[16]		
Units: score on a scale				
least squares mean (confidence interval 95%)				
Global Health Status/QOL: Cycle 4	1.35 (-0.24 to 2.94)	-0.45 (-2.04 to 1.13)		
Global Health Status/QOL: Cycle 6	0.93 (-0.71 to 2.57)	-1.58 (-3.24 to 0.07)		

Physical Functioning: Cycle 4	-2.47 (-3.77 to -1.18)	-3.92 (-5.21 to -2.62)		
Physical Functioning: Cycle 6	-2.76 (-4.22 to -1.30)	-5.22 (-6.69 to -3.75)		

Notes:

[15] - ITT Analysis Set who completed the EORTC QLQ-C30 at baseline;
Cycle 4 N=388;
Cycle 6 N=359.
[16] - ITT Analysis Set who completed the EORTC QLQ-C30 at baseline;
Cycle 4 N=380;
Cycle 6 N=339.

Statistical analyses

Statistical analysis title	Analysis of Global Health Status/QoL at Cycle 4

Statistical analysis description:

Least square (LS) mean score changes from baseline were assessed using a mixed effect model with QLQ-C30 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Placebo + Chemotherapy v Tislelizumab + Chemotherapy
Number of subjects included in analysis	932
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	-0.33
upper limit	3.94

Statistical analysis title	Analysis of Global Health Status/QoL at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-C30 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	2.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	4.74

Statistical analysis title	Analysis of Physical Functioning at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-C30 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	3.16

Statistical analysis title	Analysis of Physical Functioning at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-C30 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	4.43

Secondary: Change From Baseline in EORTC QLQ-C30 Fatigue Score

End point title	Change From Baseline in EORTC QLQ-C30 Fatigue Score

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 to a 0 to 100 scale via linear transformation. The fatigue symptom scale includes 3 items and ranges from 0 to 100, where higher scores indicate a higher level of symptoms.
Participants in the ITT Analysis Set with available data at baseline and each postbaseline visit are included.

End point type	Secondary

End point timeframe:

Baseline and Cycle 4 (Week 12) and Cycle 6

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	465[17]	467[18]		
Units: score on a scale				
least squares mean (confidence interval 95%)				
Cycle 4	1.75 (-0.09 to 3.60)	3.07 (1.23 to 4.91)		
Cycle 6	1.71 (-0.32 to 3.75)	4.73 (2.68 to 6.77)		

Notes:

[17] - ITT Analysis Set who completed the EORTC QLQ-C30 at baseline;
Cycle 4 N=388;
Cycle 6 N=359.

[18] - ITT Analysis Set who completed the EORTC QLQ-C30 at baseline;
Cycle 4 N=380;
Cycle 6 N=339.

Statistical analyses

Statistical analysis title	Analysis of Fatigue at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-C30 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.79
upper limit	1.15

Statistical analysis title	Analysis of Fatigue at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-C30 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy

Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.78
upper limit	-0.24

Secondary: Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Gastric Cancer Module QLQ-STO22 (EORTC QLQ-STO22)

End point title	Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Gastric Cancer Module QLQ-STO22 (EORTC QLQ-STO22)

End point description:

EORTC-QLQ-STO22 is a 22-item questionnaire developed to assess QoL of gastric cancer participants. It consists of 5 multi-item subscales: Dysphagia/odynophagia (4 items), Pain/discomfort (3 items), Dietary restrictions (5 items), Upper gastro-intestinal (GI) symptoms (3 items), Specific emotional problems (3 items) and 4 single items. Each question is answered on a scale from 0 (Not at all) to 4 (Very Much), where lower scores indicate fewer symptoms/better QoL.
Raw scores were transformed to a scale from 0 to 100, where lower scores indicate better QoL.
The QLQ-STO22 Index score is the mean of the 6 domain scores and 4 single items.
Participants in the ITT Analysis Set with available data at baseline and each postbaseline visit are included in the analysis.

End point type	Secondary

End point timeframe:

Baseline and Cycle 4 (Week 12) and Cycle 6 (Week 18)

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	465[19]	467[20]		
Units: score on a scale				
least squares mean (confidence interval 95%)				
Index Score: Cycle 4	-1.71 (-2.77 to -0.66)	-0.61 (-1.66 to 0.45)		
Index Score: Cycle 6	-1.84 (-2.95 to -0.74)	-0.22 (-1.34 to 0.89)		
Dysphagia/Odynophagia Scale: Cycle 4	-2.78 (-3.99 to -1.57)	-1.27 (-2.48 to -0.06)		
Dysphagia/Odynophagia Scale: Cycle 6	-2.79 (-3.93 to -1.64)	-2.01 (-3.17 to -0.86)		
Pain/Discomfort Scale: Cycle 4	-6.88 (-8.39 to -5.36)	-4.64 (-6.16 to -3.13)		
Pain/Discomfort Scale: Cycle 6	-5.97 (-7.56 to -4.38)	-4.09 (-5.69 to -2.49)		
Dietary Restrictions Scale: Cycle 4	-0.31 (-1.75 to 1.12)	0.61 (-0.82 to 2.05)		

Dietary Restrictions Scale: Cycle 6	-0.25 (-1.79 to 1.30)	1.08 (-0.48 to 2.63)		
Upper Gastro-Intestinal Symptoms: Cycle 4	-3.14 (-4.40 to -1.87)	-1.54 (-2.80 to -0.28)		
Upper Gastro-Intestinal Symptoms: Cycle 6	-3.24 (-4.58 to -1.90)	-1.49 (-2.84 to -0.14)		

Notes:

[19] - ITT Analysis Set who completed the EORTC QLQ-STO22 at baseline;
Cycle 4: N=387;
Cycle 6: N=358.

[20] - ITT Analysis Set who completed the EORTC QLQ-STO22 at baseline;
Cycle 4: N=379;
Cycle 6: N=339.

Statistical analyses

Statistical analysis title	Analysis of QLQ-STO22 Index-Score at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.53
upper limit	0.31

Statistical analysis title	Analysis of QLQ-STO22 Index-Score at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.12
upper limit	-0.12

Statistical analysis title	Analysis of Dysphagia/Odynophagia Scale at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.13
upper limit	0.11

Statistical analysis title	Analysis of Dysphagia/Odynophagia Scale at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.31
upper limit	0.76

Statistical analysis title	Analysis of Pain/Discomfort Scale at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-2.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.26
upper limit	-0.2

Statistical analysis title	Analysis of Pain/Discomfort Scale at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.03
upper limit	0.27

Statistical analysis title	Analysis of Dietary Restrictions Scale at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.85
upper limit	0.99

Statistical analysis title	Analysis of Dietary Restrictions Scale at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.42
upper limit	0.77

Statistical analysis title	Analysis of Upper GI Symptoms at Cycle 4

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.28
upper limit	0.09

Statistical analysis title	Analysis of Upper GI Symptoms at Cycle 6

Statistical analysis description:

LS mean score changes from baseline were assessed using a mixed effect model with QLQ-STO22 scores from cycle 1 to 6 as the response variable, and treatment by study visit interaction, baseline mean score and randomization stratification factors as covariates.

Comparison groups	Tislelizumab + Chemotherapy v Placebo + Chemotherapy
Number of subjects included in analysis	932
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.55
upper limit	0.06

Secondary: Change From Baseline in European Quality of Life 5-Dimensions, 5-level (EQ-5D-5L) Visual Analogue Scale (VAS)

End point title	Change From Baseline in European Quality of Life 5-Dimensions, 5-level (EQ-5D-5L) Visual Analogue Scale (VAS)

End point description:

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.
Participants in the ITT Analysis Set with available data at baseline and each postbaseline visit are included in the analysis.

End point type	Secondary

End point timeframe:

Baseline and Cycle 4 (Week 12) and Cycle 6 (Week 18)

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	465[21]	467[22]		
Units: score on a scale				
arithmetic mean (standard deviation)				
Cycle 4	2.9 (± 15.62)	0.8 (± 14.91)		
Cycle 6	3.0 (± 16.38)	-0.8 (± 15.17)		

Notes:

[21] - ITT Analysis Set who completed the EQ-5D-5L at baseline;
Cycle 4: N=360;
Cycle 6: N=331
[22] - ITT Analysis Set who completed the EQ-5D-5L at baseline;
Cycle 4: N=364;
Cycle 6: N=322

Statistical analyses

No statistical analyses for this end point

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 untoward medical occurrence that, at any dose met any of the following criteria:
- 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 based on medical judgement.

The Safety Analysis Set included all participants who received ≥ 1 dose of study drug

End point type	Secondary

End point timeframe:

From first dose of study drug to 30 days after last dose or the initiation of a new anticancer therapy, whichever occurred first, up to the end of study; maximum treatment duration was 59.3 months in Tislelizumab and 56.8 months in the Placebo group.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	498[23]	494[24]		
Units: participants				
Any TEAE	495	486		
Any SAE	211	179		

Notes:

[23] - Safety Analysis Set

[24] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate in PD-L1 Positive Participants

End point title	Disease Control Rate in PD-L1 Positive Participants

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 investigator and the investigator per RECIST v1.1. Investigators conducted assessments of radiological tumor response by CT or MRI per RECIST version 1.1 about every six weeks during the first 48 weeks of the study and every nine weeks thereafter.
CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits.
SD: Neither sufficient shrinkage in size of lesions to qualify for PR nor sufficient increase to qualify for PD, and no new lesions.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[25]	272[26]		
Units: percentage of participants				
number (confidence interval 95%)	88.3 (83.9 to 91.9)	83.1 (78.1 to 87.3)		

Notes:

[25] - PD-L1 Positive Analysis Set

[26] - PD-L1 Positive Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate in the ITT Analysis Set

End point title	Disease Control Rate in the ITT Analysis Set

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 investigator per RECIST v1.1. Investigators conducted assessments of radiological tumor response by CT or MRI per RECIST version 1.1 about every six weeks during the first 48 weeks of the study and every nine weeks thereafter.
CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits.
SD: Neither sufficient shrinkage in size of lesions to qualify for PR nor sufficient increase to qualify for PD, and no new lesions.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	501	496		
Units: percentage of participants				
number (confidence interval 95%)	89.8 (86.8 to 92.3)	83.3 (79.7 to 86.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) in PD-L1 Positive Participants

End point title	Clinical Benefit Rate (CBR) in PD-L1 Positive Participants

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 Investigator per RECIST v1.1.
CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits.
Durable SD: Stable disease for ≥ 24 weeks.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[27]	272[28]		
Units: percentage of participants				
number (confidence interval 95%)	65.0 (59.0 to 70.6)	59.2 (53.1 to 65.1)		

Notes:

[27] - PD-L1 Positive Analysis Set

[28] - PD-L1 Positive Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) in the ITT Analysis Set

End point title	Clinical Benefit Rate (CBR) in the ITT Analysis Set

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 Investigator per RECIST v1.1.
CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits.
Durable SD: Stable disease for ≥ 24 weeks.

End point type	Secondary

End point timeframe:

Response was assessed every 6 weeks for the first 48 weeks and every 9 weeks thereafter; up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	501	496		
Units: percentage of participants				
number (confidence interval 95%)	63.1 (58.7 to 67.3)	58.9 (54.4 to 63.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) in PD-L1 Positive Participants

End point title	Time to Response (TTR) in PD-L1 Positive Participants

End point description:

Time to response is defined as the time from randomization to the first determination of an objective response per RECIST version 1.1 as assessed by the investigator.
The analysis includes participants in the PD-L1 Positive Analysis Set with an objective response.

End point type	Secondary

End point timeframe:

From randomization up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141[29]	116[30]		
Units: months				
median (full range (min-max))	1.4 (0.9 to 11.3)	1.4 (1.0 to 17.5)		

Notes:

[29] - PD-L1 Positive Analysis Set with an objective response

[30] - PD-L1 Positive Analysis Set with an objective response

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) in the ITT Analysis Set

End point title	Time to Response (TTR) in the ITT Analysis Set

End point description:

Time to response is defined as the time from randomization to the first determination of an objective response per RECIST version 1.1 as assessed by the investigator.
The analysis includes participants in the ITT Analysis Set with an objective response.

End point type	Secondary

End point timeframe:

From randomization up to the final efficacy analysis data cut-off date of 28 February 2023; Median (range) time on follow-up was 13.2 (0.1 - 50.1) months.

End point values	Tislelizumab + Chemotherapy	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237[31]	201[32]		
Units: months				
median (full range (min-max))	1.4 (0.9 to 13.4)	1.4 (1.0 to 17.5)		

Notes:

[31] - ITT Analysis Set with an objective response

[32] - ITT Analysis Set with an objective response

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug to 30 days after last dose or the initiation of a new anticancer therapy, whichever occurred first, up to the end of study; maximum treatment duration was 59.3 months in Tislelizumab and 56.8 months in the Placebo group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo + Chemotherapy

Reporting group description:

Participants received placebo intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Thereafter, participants continued treatment with placebo once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.

Reporting group title	Tislelizumab + Chemotherapy

Reporting group description:

Participants received 200 mg of tislelizumab intravenously with investigator's choice of chemotherapy once every 3 weeks for up to six treatment cycles. Thereafter, participants continued treatment with 200 mg tislelizumab once every 3 weeks, with optional maintenance capecitabine (only permitted for participants who initially received capecitabine and oxaliplatin) until disease progression or unacceptable toxicity.

Serious adverse events	Placebo + Chemotherapy	Tislelizumab + Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	179 / 494 (36.23%)	211 / 498 (42.37%)	
number of deaths (all causes)	429	397	
number of deaths resulting from adverse events	42	47	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant ascites			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			
subjects affected / exposed	2 / 494 (0.40%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastases to spine			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tumour thrombotic microangiopathy			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	4 / 494 (0.81%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			

subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brachiocephalic vein thrombosis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 494 (0.40%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism arterial			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Shock haemorrhagic			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Death			

subjects affected / exposed	5 / 494 (1.01%)	10 / 498 (2.01%)	
occurrences causally related to treatment / all	0 / 5	4 / 10	
deaths causally related to treatment / all	0 / 5	4 / 10	
Device related thrombosis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 494 (0.20%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	1 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	7 / 494 (1.42%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 7	1 / 6	
deaths causally related to treatment / all	0 / 7	1 / 6	
Generalised oedema			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 494 (0.40%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyserositis			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	6 / 494 (1.21%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	1 / 6	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthenia			
subjects affected / exposed	2 / 494 (0.40%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	2 / 494 (0.40%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated adverse reaction			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Immune-mediated lung disease			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Aspiration			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hiccups			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	3 / 494 (0.61%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 494 (0.40%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 494 (0.00%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	4 / 494 (0.81%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 5	
deaths causally related to treatment / all	0 / 3	0 / 2	
Pulmonary infarction			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 494 (0.00%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Nasal polyps			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 494 (0.00%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 494 (0.20%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	1 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrin D dimer increased			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrin degradation products increased			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	17 / 494 (3.44%)	16 / 498 (3.21%)	
occurrences causally related to treatment / all	21 / 21	21 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 494 (0.20%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic stenosis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heat illness			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Remnant gastritis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Sinus arrest			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 494 (0.40%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
IIIrd nerve paralysis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 494 (0.40%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 494 (2.02%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	7 / 10	4 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	4 / 494 (0.81%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	3 / 494 (0.61%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extraocular muscle paresis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cataract subcapsular			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Appendicitis noninfective			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	4 / 494 (0.81%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	3 / 5	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	2 / 494 (0.40%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal adhesions			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 494 (0.40%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	1 / 2	
Gastritis			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric stenosis			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	1 / 494 (0.20%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Gastric haemorrhage			
subjects affected / exposed	1 / 494 (0.20%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 3	
Enterocolitis			

subjects affected / exposed	3 / 494 (0.61%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	4 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	3 / 494 (0.61%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 494 (0.81%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	5 / 5	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	3 / 494 (0.61%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Bezoar			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	5 / 494 (1.01%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 3	
Ileus			

subjects affected / exposed	4 / 494 (0.81%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stenosis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	7 / 494 (1.42%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	1 / 8	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Volvulus of small bowel			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	3 / 494 (0.61%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	1 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic enteritis			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 494 (0.20%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	2 / 494 (0.40%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric panniculitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	5 / 494 (1.01%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	3 / 5	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	5 / 494 (1.01%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Oesophageal food impaction			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal obstruction			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			

subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal stenosis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	3 / 494 (0.61%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	5 / 494 (1.01%)	7 / 498 (1.41%)	
occurrences causally related to treatment / all	5 / 5	7 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	1 / 494 (0.20%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	1 / 1	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	3 / 494 (0.61%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 494 (0.20%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder obstruction			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 494 (0.20%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hepatic function abnormal			

subjects affected / exposed	1 / 494 (0.20%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 494 (0.20%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	4 / 494 (0.81%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	
Liver injury			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venoocclusive liver disease			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 494 (0.40%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	2 / 2	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated renal disorder			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 494 (0.20%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Ureteric obstruction			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
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 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			

subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated myositis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint adhesion			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bacteraemia			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	2 / 494 (0.40%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 494 (0.40%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 494 (0.00%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			

subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	14 / 494 (2.83%)	12 / 498 (2.41%)	
occurrences causally related to treatment / all	6 / 18	1 / 13	
deaths causally related to treatment / all	2 / 2	0 / 1	
Pyelonephritis			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash pustular			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	2 / 494 (0.40%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 2	3 / 6	
deaths causally related to treatment / all	0 / 1	2 / 4	
Septic shock			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Hypoproteinaemia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cachexia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Decreased appetite			
subjects affected / exposed	5 / 494 (1.01%)	7 / 498 (1.41%)	
occurrences causally related to treatment / all	4 / 5	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 494 (0.20%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 494 (0.20%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	2 / 494 (0.40%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Latent autoimmune diabetes in adults			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 494 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo + Chemotherapy	Tislelizumab + Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	485 / 494 (98.18%)	489 / 498 (98.19%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	23 / 494 (4.66%)	12 / 498 (2.41%)	
occurrences (all)	31	21	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	86 / 494 (17.41%)	97 / 498 (19.48%)	
occurrences (all)	116	121	
Chest discomfort			
subjects affected / exposed	11 / 494 (2.23%)	15 / 498 (3.01%)	
occurrences (all)	18	17	
Chills			
subjects affected / exposed	7 / 494 (1.42%)	20 / 498 (4.02%)	
occurrences (all)	7	26	
Fatigue			
subjects affected / exposed	73 / 494 (14.78%)	87 / 498 (17.47%)	
occurrences (all)	101	105	
Malaise			
subjects affected / exposed	41 / 494 (8.30%)	37 / 498 (7.43%)	
occurrences (all)	49	45	
Oedema peripheral			
subjects affected / exposed	38 / 494 (7.69%)	41 / 498 (8.23%)	
occurrences (all)	42	48	
Pyrexia			
subjects affected / exposed	66 / 494 (13.36%)	99 / 498 (19.88%)	
occurrences (all)	92	185	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	32 / 494 (6.48%)	25 / 498 (5.02%)	
occurrences (all)	38	34	

Dyspnoea			
subjects affected / exposed	33 / 494 (6.68%)	29 / 498 (5.82%)	
occurrences (all)	41	37	
Hiccups			
subjects affected / exposed	16 / 494 (3.24%)	20 / 498 (4.02%)	
occurrences (all)	23	23	
Productive cough			
subjects affected / exposed	20 / 494 (4.05%)	31 / 498 (6.22%)	
occurrences (all)	24	36	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	53 / 494 (10.73%)	47 / 498 (9.44%)	
occurrences (all)	65	51	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	105 / 494 (21.26%)	123 / 498 (24.70%)	
occurrences (all)	175	188	
Aspartate aminotransferase increased			
subjects affected / exposed	150 / 494 (30.36%)	157 / 498 (31.53%)	
occurrences (all)	274	285	
Blood alkaline phosphatase increased			
subjects affected / exposed	22 / 494 (4.45%)	19 / 498 (3.82%)	
occurrences (all)	25	33	
Blood bilirubin increased			
subjects affected / exposed	74 / 494 (14.98%)	75 / 498 (15.06%)	
occurrences (all)	172	171	
Blood creatine phosphokinase increased			
subjects affected / exposed	20 / 494 (4.05%)	17 / 498 (3.41%)	
occurrences (all)	32	30	
Blood creatinine increased			
subjects affected / exposed	14 / 494 (2.83%)	15 / 498 (3.01%)	
occurrences (all)	16	22	
Blood lactate dehydrogenase increased			
subjects affected / exposed	20 / 494 (4.05%)	18 / 498 (3.61%)	
occurrences (all)	33	36	

Gamma-glutamyltransferase increased			
subjects affected / exposed	22 / 494 (4.45%)	19 / 498 (3.82%)	
occurrences (all)	27	31	
Lymphocyte count decreased			
subjects affected / exposed	22 / 494 (4.45%)	28 / 498 (5.62%)	
occurrences (all)	45	67	
Neutrophil count decreased			
subjects affected / exposed	163 / 494 (33.00%)	172 / 498 (34.54%)	
occurrences (all)	573	705	
Platelet count decreased			
subjects affected / exposed	184 / 494 (37.25%)	173 / 498 (34.74%)	
occurrences (all)	390	384	
Weight decreased			
subjects affected / exposed	102 / 494 (20.65%)	110 / 498 (22.09%)	
occurrences (all)	122	139	
Weight increased			
subjects affected / exposed	9 / 494 (1.82%)	28 / 498 (5.62%)	
occurrences (all)	9	36	
White blood cell count decreased			
subjects affected / exposed	136 / 494 (27.53%)	120 / 498 (24.10%)	
occurrences (all)	488	580	
Nervous system disorders			
Dizziness			
subjects affected / exposed	42 / 494 (8.50%)	41 / 498 (8.23%)	
occurrences (all)	52	54	
Headache			
subjects affected / exposed	19 / 494 (3.85%)	20 / 498 (4.02%)	
occurrences (all)	21	23	
Hypoaesthesia			
subjects affected / exposed	69 / 494 (13.97%)	70 / 498 (14.06%)	
occurrences (all)	110	99	
Neurotoxicity			
subjects affected / exposed	16 / 494 (3.24%)	13 / 498 (2.61%)	
occurrences (all)	27	23	
Paraesthesia			

subjects affected / exposed	18 / 494 (3.64%)	12 / 498 (2.41%)	
occurrences (all)	25	12	
Peripheral sensory neuropathy			
subjects affected / exposed	118 / 494 (23.89%)	106 / 498 (21.29%)	
occurrences (all)	156	134	
Dysgeusia			
subjects affected / exposed	18 / 494 (3.64%)	25 / 498 (5.02%)	
occurrences (all)	18	29	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	202 / 494 (40.89%)	197 / 498 (39.56%)	
occurrences (all)	355	374	
Neutropenia			
subjects affected / exposed	82 / 494 (16.60%)	75 / 498 (15.06%)	
occurrences (all)	184	247	
Thrombocytopenia			
subjects affected / exposed	56 / 494 (11.34%)	64 / 498 (12.85%)	
occurrences (all)	101	131	
Leukopenia			
subjects affected / exposed	45 / 494 (9.11%)	44 / 498 (8.84%)	
occurrences (all)	123	193	
Eye disorders			
Cataract			
subjects affected / exposed	22 / 494 (4.45%)	18 / 498 (3.61%)	
occurrences (all)	25	21	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	8 / 494 (1.62%)	16 / 498 (3.21%)	
occurrences (all)	9	23	
Abdominal distension			
subjects affected / exposed	52 / 494 (10.53%)	53 / 498 (10.64%)	
occurrences (all)	59	61	
Abdominal pain			
subjects affected / exposed	80 / 494 (16.19%)	75 / 498 (15.06%)	
occurrences (all)	97	109	
Abdominal pain upper			

subjects affected / exposed	55 / 494 (11.13%)	51 / 498 (10.24%)	
occurrences (all)	80	62	
Ascites			
subjects affected / exposed	9 / 494 (1.82%)	18 / 498 (3.61%)	
occurrences (all)	10	18	
Constipation			
subjects affected / exposed	105 / 494 (21.26%)	90 / 498 (18.07%)	
occurrences (all)	144	123	
Diarrhoea			
subjects affected / exposed	144 / 494 (29.15%)	134 / 498 (26.91%)	
occurrences (all)	241	223	
Dry mouth			
subjects affected / exposed	9 / 494 (1.82%)	23 / 498 (4.62%)	
occurrences (all)	9	28	
Dyspepsia			
subjects affected / exposed	28 / 494 (5.67%)	21 / 498 (4.22%)	
occurrences (all)	37	21	
Dysphagia			
subjects affected / exposed	17 / 494 (3.44%)	21 / 498 (4.22%)	
occurrences (all)	20	23	
Gastrooesophageal reflux disease			
subjects affected / exposed	26 / 494 (5.26%)	17 / 498 (3.41%)	
occurrences (all)	38	20	
Nausea			
subjects affected / exposed	237 / 494 (47.98%)	248 / 498 (49.80%)	
occurrences (all)	443	469	
Stomatitis			
subjects affected / exposed	35 / 494 (7.09%)	37 / 498 (7.43%)	
occurrences (all)	44	47	
Vomiting			
subjects affected / exposed	178 / 494 (36.03%)	176 / 498 (35.34%)	
occurrences (all)	352	330	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	93 / 494 (18.83%)	95 / 498 (19.08%)	
occurrences (all)	111	107	
Pruritus			
subjects affected / exposed	15 / 494 (3.04%)	52 / 498 (10.44%)	
occurrences (all)	19	65	
Rash			
subjects affected / exposed	17 / 494 (3.44%)	43 / 498 (8.63%)	
occurrences (all)	19	52	
Skin hyperpigmentation			
subjects affected / exposed	14 / 494 (2.83%)	20 / 498 (4.02%)	
occurrences (all)	16	21	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	13 / 494 (2.63%)	63 / 498 (12.65%)	
occurrences (all)	13	73	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 494 (4.86%)	23 / 498 (4.62%)	
occurrences (all)	26	26	
Back pain			
subjects affected / exposed	40 / 494 (8.10%)	30 / 498 (6.02%)	
occurrences (all)	46	35	
Myalgia			
subjects affected / exposed	18 / 494 (3.64%)	14 / 498 (2.81%)	
occurrences (all)	20	15	
Pain in extremity			
subjects affected / exposed	22 / 494 (4.45%)	18 / 498 (3.61%)	
occurrences (all)	23	22	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 494 (2.83%)	20 / 498 (4.02%)	
occurrences (all)	14	27	
Pneumonia			
subjects affected / exposed	13 / 494 (2.63%)	19 / 498 (3.82%)	
occurrences (all)	14	19	
Upper respiratory tract infection			

subjects affected / exposed	13 / 494 (2.63%)	25 / 498 (5.02%)	
occurrences (all)	15	34	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	207 / 494 (41.90%)	202 / 498 (40.56%)	
occurrences (all)	327	277	
Hyperglycaemia			
subjects affected / exposed	15 / 494 (3.04%)	13 / 498 (2.61%)	
occurrences (all)	23	17	
Hypoalbuminaemia			
subjects affected / exposed	92 / 494 (18.62%)	87 / 498 (17.47%)	
occurrences (all)	130	147	
Hypocalcaemia			
subjects affected / exposed	11 / 494 (2.23%)	22 / 498 (4.42%)	
occurrences (all)	15	24	
Hypokalaemia			
subjects affected / exposed	57 / 494 (11.54%)	84 / 498 (16.87%)	
occurrences (all)	89	152	
Hyponatraemia			
subjects affected / exposed	31 / 494 (6.28%)	36 / 498 (7.23%)	
occurrences (all)	38	54	
Hypoproteinaemia			
subjects affected / exposed	25 / 494 (5.06%)	21 / 498 (4.22%)	
occurrences (all)	38	25	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2018	• Increased sample size from 640 to 720 patients. • Added PFS after next line of treatment (PFS2) for the exploratory efficacy analysis, defined as the time from randomization to the objective disease progression after next line of treatment or death from any cause, whichever occurred first. • Modified the description of exploratory biomarkers to "including, but not limited to, PD-L1 expression, Epstein-Barr virus (EBV) infection, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) status, genomically stable (GS) or chromosomal instability (CIN), immune-related gene expression profiling, tumor infiltrated lymphocytes (TILs), and tumor mutation burden in tumor tissues and/or blood samples." • Clarified that the patients whose tumors were PD-L1 positive with PD-L1 score ≥ 5% using VENTANA PD-L1 (SP263) Assay. PD-L1 score (previously referred to TIC score in protocol) was the total percentage of the tumor area covered by tumor cells with PD-L1 membrane staining and tumor-associated immune cells with PD-L1 staining at any intensity. • Adjusted the 1-sided alpha of 0.00275 to 0.0025 for the primary efficacy analyses of PFS in the PD-L1 Positive and ITT Analysis Sets. • Adjusted the 1-sided alpha of 0.011 to 0.01 for the primary efficacy analyses of OS in the PD-L1 Positive and ITT Analysis Sets.
03 April 2020	• Moved assessment of PFS from primary objective/endpoint to secondary objective/endpoint. • Removed IRC and IRC related efficacy objectives/endpoints. • Moved assessment of DCR, CBR, and TTR from exploratory objectives/endpoints to secondary objectives/endpoints. • Revised to compare OS of tislelizumab plus chemotherapy versus the placebo plus chemotherapy in the PD-L1 Positive Analysis Set first and then in the ITT Analysis Set. • Added third-party local laboratory that was eligible to perform unavailable MSI/MMR status, an MSI/MMR assessment, or HER2 test in addition to investigational sites or designated central laboratory per the US FDA's commitment. • Revised "Patients should notify the investigator of the decision to withdraw consent from future follow-up in writing, if possible" to "Patients should notify the investigator of the decision to withdraw consent from future follow-up verbally or in writing" per South Korea EC's comment to meet the standard site practice. • Updated sample size consideration per the update in primary endpoint, PD-L1 prevalence rate, and hazard ratio assumption. • Updated the inclusion criteria to allow patients with non-target lesion only to be enrolled.
17 April 2023	• Added a statement regarding unblinding investigators, site personnel, and patients to the treatment arms and PD-L1 results at the time of final analysis. • Clarified the reconsent process per ICH-GCP and local regulations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported