# 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<br>Units: Subjects | | | |
| Between 18 and 65 years | 340 | 313 | 653 |
| >=65 years | 161 | 183 | 344 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 58.8 | 59.7 | |
| standard deviation | ± 11.07 | ± 11.20 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 155 | 150 | 305 |
| Male | 346 | 346 | 692 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | 6 | 8 |
| Not Hispanic or Latino | 492 | 474 | 966 |
| Unknown or Not Reported | 7 | 16 | 23 |
| Race<br>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<br>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<br>Units: Subjects | | | |
| Yes | 220 | 214 | 434 |
| No | 281 | 282 | 563 |
| Investigator Chosen Chemotherapy<br>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.<br>• 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.<br>• 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."<br>• 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.<br>• 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.<br>• 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.<br>• Removed IRC and IRC related efficacy objectives/endpoints.<br>• Moved assessment of DCR, CBR, and TTR from exploratory objectives/endpoints to secondary objectives/endpoints.<br>• 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.<br>• 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.<br>• 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.<br>• Updated sample size consideration per the update in primary endpoint, PD-L1 prevalence rate, and hazard ratio assumption.<br>• 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.<br>• 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