



## Clinical trial results:

### A Phase II, Randomized, Double-Blind Placebo-Controlled Study of Atezolizumab With or Without Bevacizumab in Combination With Cisplatin Plus Gemcitabine in Patients With Untreated, Advanced Biliary Tract Cancer

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-003759-14 |
| Trial protocol           | PL IT          |
| Global end of trial date |                |

#### Results information

|                                |             |
|--------------------------------|-------------|
| Result version number          | v1          |
| This version publication date  | 27 May 2023 |
| First version publication date | 27 May 2023 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | GO42661 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04677504 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | F. Hoffmann-La Roche AG  |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070   |
| Public contact               | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact           | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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                                       | Interim     |
| Date of interim/final analysis                       | 16 May 2022 |
| Is this the analysis of the primary completion data? | Yes         |
| Primary completion date                              | 16 May 2022 |
| Global end of trial reached?                         | No          |

Notes:

## General information about the trial

Main objective of the trial:

This study evaluated the efficacy and safety of atezolizumab with bevacizumab in combination with cisplatin and gemcitabine (CisGem), compared with atezolizumab in combination with CisGem, in participants with advanced biliary tract cancer (BTC) (i.e., intrahepatic cholangiocarcinoma [iCCA], extrahepatic CCA [eCCA], or gallbladder cancer [GBC]) who did not received prior systemic therapy.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 23 February 2021 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | China: 6               |
| Country: Number of subjects enrolled | Spain: 11              |
| Country: Number of subjects enrolled | United Kingdom: 9      |
| Country: Number of subjects enrolled | Hong Kong: 2           |
| Country: Number of subjects enrolled | Italy: 17              |
| Country: Number of subjects enrolled | Korea, Republic of: 44 |
| Country: Number of subjects enrolled | Poland: 11             |
| Country: Number of subjects enrolled | Russian Federation: 16 |
| Country: Number of subjects enrolled | Thailand: 8            |
| Country: Number of subjects enrolled | Turkey: 8              |
| Country: Number of subjects enrolled | Taiwan: 9              |
| Country: Number of subjects enrolled | Ukraine: 7             |
| Country: Number of subjects enrolled | United States: 14      |
| Worldwide total number of subjects   | 162                    |
| EEA total number of subjects         | 39                     |

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)                      | 89 |
| From 65 to 84 years                       | 73 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This is a global multicenter study.

### Pre-assignment

Screening details:

This study included participants with advanced biliary tract cancer (i.e., intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer) who did not receive prior systemic therapy.

### 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          |

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO |

Arm description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Atezolizumab      |
| Investigational medicinal product code |                   |
| Other name                             | Tecentriq         |
| Pharmaceutical forms                   | Infusion          |
| Routes of administration               | Intravenous use   |

Dosage and administration details:

Atezolizumab was administered intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Gemcitabine was administered intravenously at a dose of 1000 mg/m<sup>2</sup> on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Cisplatin       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Cisplatin was administered intravenously at a dose of 25 mg/m<sup>2</sup> on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Placebo         |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Placebo matching bevacizumab was administered intravenously on Day 1 of each 21-day cycle after atezolizumab.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |
|------------------|--|

**Arm description:**

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Atezolizumab    |
| Investigational medicinal product code |                 |
| Other name                             | Tecentriq       |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Atezolizumab was administered intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Gemcitabine was administered intravenously at a dose of 1000 mg/m<sup>2</sup> on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Cisplatin       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Cisplatin was administered intravenously at a dose of 25 mg/m<sup>2</sup> on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Bevacizumab     |
| Investigational medicinal product code |                 |
| Other name                             | Avastin         |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Bevacizumab was administered at a dose of 15 mg/kg intravenously on Day 1 of each 21-day cycle after atezolizumab.

| <b>Number of subjects in period 1</b> | <b>Arm B:<br/>Atezo+PBO+CisGem<br/>, followed by<br/>Atezo+PBO</b> | <b>Arm A:<br/>Atezo+Bev+CisGem,<br/>followed by<br/>Atezo+Bev</b> |
|---------------------------------------|--|---|
| Started                               | 83   | 79  |
| Completed                             | 0  | 0   |
| Not completed                         | 83   | 79  |
| Adverse event, serious fatal          | 31   | 24  |
| Consent withdrawn by subject          | 2  | 5   |
| Ongoing in study                      | 48   | 50  |
| Progressive Disease                   | 1  | -   |
| Symptomatic Deterioration             | 1  | -   |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO |
|-----------------------|--|

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|                       |  |
|-----------------------|--|
| Reporting group title | Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |
|-----------------------|--|

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

| Reporting group values                                | Arm B:<br>Atezo+PBO+CisGem<br>, followed by<br>Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem,<br>followed by<br>Atezo+Bev | Total |
|---|--|---|-------|
| Number of subjects                                    | 83   | 79  | 162   |
| Age categorical<br>Units: Subjects                    |  |   |       |
| In utero  | 0  | 0   | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0  | 0   | 0     |
| Newborns (0-27 days)                                  | 0  | 0   | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0  | 0   | 0     |
| Children (2-11 years)                                 | 0  | 0   | 0     |
| Adolescents (12-17 years)                             | 0  | 0   | 0     |
| Adults (18-64 years)                                  | 38   | 51  | 89    |
| From 65-84 years                                      | 45   | 28  | 73    |
| 85 years and over                                     | 0  | 0   | 0     |
| Age Continuous<br>Units: Years                        |  |   |       |
| arithmetic mean                                       | 63.0   | 59.6  |       |
| standard deviation                                    | ± 9.8  | ± 9.9   | -     |
| Sex: Female, Male<br>Units:                           |  |   |       |
| Female  | 45   | 30  | 75    |
| Male  | 38   | 49  | 87    |
| Race (NIH/OMB)<br>Units: Subjects                     |  |   |       |
| American Indian or Alaska Native                      | 0  | 0   | 0     |
| Asian   | 35   | 37  | 72    |
| Native Hawaiian or Other Pacific<br>Islander          | 0  | 0   | 0     |
| Black or African American                             | 1  | 1   | 2     |
| White   | 46   | 41  | 87    |
| More than one race                                    | 0  | 0   | 0     |

|                         |    |    |     |
|-------------------------|----|----|-----|
| Unknown or Not Reported | 1  | 0  | 1   |
| Ethnicity (NIH/OMB)     |    |    |     |
| Units: Subjects         |    |    |     |
| Hispanic or Latino      | 1  | 1  | 2   |
| Not Hispanic or Latino  | 82 | 78 | 160 |
| Unknown or Not Reported | 0  | 0  | 0   |



## End points

### End points reporting groups

|   |  |
|---|--|
| Reporting group title   | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO |
| Reporting group description:<br>Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8. |  |
| Reporting group title   | Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |
| Reporting group description:<br>Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.                  |  |

### Primary: Progression Free Survival (PFS)

|  |                                 |
|--|---------------------------------|
| End point title  | Progression Free Survival (PFS) |
| End point description:<br>PFS is defined as the time from randomization to the first occurrence of disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first) |                                 |
| End point type   | Primary                         |
| End point timeframe:<br>Randomization to the first occurrence of disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first)(up to approximately 14 months)    |                                 |

| End point values                 | Arm B:<br>Atezo+PBO+CisGem, followed by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed by Atezo+Bev |  |  |
|----------------------------------|---|---|--|--|
| Subject group type               | Reporting group                                   | Reporting group                                   |  |  |
| Number of subjects analysed      | 83  | 79  |  |  |
| Units: Months                    |   |   |  |  |
| median (confidence interval 95%) | 7.92 (6.18 to 8.41)                               | 8.35 (6.83 to 9.96)                               |  |  |

### Statistical analyses

|  |   |
|--|---|
| Statistical analysis title   | PFS Statistical Analysis  |
| Statistical analysis description:<br>Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World). |   |
| Comparison groups  | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |

|   |                   |
|---|-------------------|
| Number of subjects included in analysis | 162               |
| Analysis specification                  | Pre-specified     |
| Analysis type                           | superiority       |
| Method                                  | Regression, Cox   |
| Parameter estimate                      | Hazard ratio (HR) |
| Point estimate                          | 0.76              |
| Confidence interval                     |                   |
| level                                   | 95 %              |
| sides                                   | 2-sided           |
| lower limit                             | 0.51              |
| upper limit                             | 1.14              |

## Secondary: Overall Survival (OS)

|                        |   |
|------------------------|---|
| End point title        | Overall Survival (OS)   |
| End point description: | OS is defined as the time from randomization to death from any cause. 999999=not estimable. |
| End point type         | Secondary   |
| End point timeframe:   | Randomization to death from any cause (up to approximately 14 months)                       |

| End point values                 | Arm B:<br>Atezo+PBO+CisGem, followed by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed by Atezo+Bev |  |  |
|----------------------------------|---|---|--|--|
| Subject group type               | Reporting group                                   | Reporting group                                   |  |  |
| Number of subjects analysed      | 83  | 79  |  |  |
| Units: Months                    |   |   |  |  |
| median (confidence interval 95%) | 11.37 (10.61 to 999999)                           | 999999 (10.97 to 999999)                          |  |  |

## Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | OS Statistical Analysis   |
| Statistical analysis description:       | Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World). |
| Comparison groups                       | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev   |
| Number of subjects included in analysis | 162   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| Method                                  | Regression, Cox   |
| Parameter estimate                      | Hazard ratio (HR)   |
| Point estimate                          | 0.74  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.43    |
| upper limit         | 1.27    |

### Secondary: Confirmed Objective Response Rate (ORR)

|  |   |
|--|---|
| End point title  | Confirmed Objective Response Rate (ORR) |
| End point description:   |   |
| Confirmed ORR is defined as the proportion of participants with Complete Response (CR) or Partial Response (PR) on two consecutive occasions $\geq 4$ weeks apart, as determined by the investigator according to RECIST v1.1. |   |
| End point type   | Secondary                               |
| End point timeframe:   |   |
| Randomization up to approximately 14 months  |   |

| End point values                  | Arm B:<br>Atezo+PBO+Cis<br>sGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+Cis<br>Gem, followed<br>by Atezo+Bev |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed       | 83  | 79   |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (not applicable)           | 25.3  | 24.1   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DOR)

|  |                            |
|--|----------------------------|
| End point title  | Duration of Response (DOR) |
| End point description:   |                            |
| DOR is defined as the time from the first occurrence of a confirmed objective response to disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first). 999999=not estimable. |                            |
| End point type   | Secondary                  |
| End point timeframe:   |                            |
| First occurrence of a confirmed objective response to disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first)(up to approximately 14 months)                             |                            |

| End point values                 | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed      | 21   | 19   |  |  |
| Units: Months                    |  |  |  |  |
| median (confidence interval 95%) | 5.78 (4.27 to 6.70)                                  | 999999 (6.44 to 999999)                              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Disease Control Rate (DCR)

|   |                            |
|---|----------------------------|
| End point title   | Disease Control Rate (DCR) |
| End point description:<br>DCR is defined as the proportion of participants with a CR or a PR on two consecutive occasions $\geq 4$ weeks apart or SD with a minimum duration of 9 weeks, as determined by the investigator according to RECIST v1.1 |                            |
| End point type  | Secondary                  |
| End point timeframe:<br>Randomization up to approximately 14 months   |                            |

| End point values                  | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed       | 83   | 79   |  |  |
| Units: Percentage of participants |  |  |  |  |
| number (not applicable)           | 75.9   | 78.5   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Confirmed Deterioration (TTCD)

|  |  |
|--|--|
| End point title  | Time to Confirmed Deterioration (TTCD) |
| End point description:<br>TTCD in patient-reported physical functioning, role functioning, and quality of life, as measured by the respective scales of the EORTC QLQ-C30 and/or EORTC IL77, and defined as the time from randomization to the first clinically meaningful deterioration that is either maintained for two consecutive assessments or followed by death from any cause within 3 weeks. 999999=not estimable. |  |
| End point type   | Secondary                              |
| End point timeframe:<br>Randomization to the first clinically meaningful deterioration (up to approximately 14 months)   |  |

| <b>End point values</b>          | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed      | 83   | 79   |  |  |
| Units: Months                    |  |  |  |  |
| median (confidence interval 95%) |  |  |  |  |
| Quality of Life                  | 6.28 (3.06 to 999999)                                | 2.79 (1.58 to 5.32)                                  |  |  |
| Physical Function Scale          | 3.29 (1.87 to 10.58)                                 | 6.21 (4.63 to 999999)                                |  |  |
| Role Function Scale              | 3.52 (2.20 to 8.51)                                  | 4.24 (2.10 to 6.28)                                  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Quality of Life Statistical Analysis  |
|---|---|
| Statistical analysis description:   |   |
| Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World). |   |
| Comparison groups   | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |
| Number of subjects included in analysis   | 162   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority   |
| Method  | Regression, Cox   |
| Parameter estimate  | Hazard ratio (HR)   |
| Point estimate  | 1.56  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.93  |
| upper limit   | 2.63  |

| <b>Statistical analysis title</b>   | Role Function Scale Statistical Analysis  |
|---|---|
| Statistical analysis description:   |   |
| Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World). |   |
| Comparison groups   | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |

|   |                   |
|---|-------------------|
| Number of subjects included in analysis | 162               |
| Analysis specification                  | Pre-specified     |
| Analysis type                           | superiority       |
| Method                                  | Regression, Cox   |
| Parameter estimate                      | Hazard ratio (HR) |
| Point estimate                          | 1.12              |
| Confidence interval                     |                   |
| level                                   | 95 %              |
| sides                                   | 2-sided           |
| lower limit                             | 0.68              |
| upper limit                             | 1.85              |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Physical Function Scale Statistical Analysis  |
| Statistical analysis description:   |   |
| Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World). |   |
| Comparison groups   | Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev |
| Number of subjects included in analysis   | 162   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority   |
| Method  | Regression, Cox   |
| Parameter estimate  | Hazard ratio (HR)   |
| Point estimate  | 0.81  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.48  |
| upper limit   | 1.36  |

## Secondary: Percentage of Participants With Adverse Events

|   |  |
|---|--|
| End point title                             | Percentage of Participants With Adverse Events |
| End point description:                      |  |
|   |  |
| End point type                              | Secondary                                      |
| End point timeframe:                        |  |
| Randomization up to approximately 3-5 years |  |

| End point values                  | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed       | 0 <sup>[1]</sup>                                     | 0 <sup>[2]</sup>                                     |  |  |
| Units: Percentage of participants |  |  |  |  |

Notes:

[1] - To be reported after end of study.

[2] - To be reported after end of study.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Concentration of Atezolizumab

|                 |                                     |
|-----------------|-------------------------------------|
| End point title | Serum Concentration of Atezolizumab |
|-----------------|-------------------------------------|

End point description:

Serum concentration of atezolizumab at specified timepoints. Note: 999999= below the level of detection.

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

End point timeframe:

Pre-Dose on Day 1 of Cycles 1, 2, 3, 4, 8, 12, and 16, and Post Dose Day 1 of Cycle 1 (cycle length=21 days)

| End point values                     | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed          | 81   | 78   |  |  |
| Units: µg/ mL                        |  |  |  |  |
| arithmetic mean (standard deviation) |  |  |  |  |
| Cycle 1 Day 1 Pre-Dose (n=74, 78)    | 999999 (± 999999)                                    | 999999 (± 999999)                                    |  |  |
| Cycle 1 Day 1 Post Dose (n=75, 80)   | 416 (± 173)  | 411 (± 73.8)   |  |  |
| Cycle 2 Day 1 Pre-Dose (n=75, 78)    | 85.0 (± 71.7)  | 79.4 (± 46.1)  |  |  |
| Cycle 3 Day 1 Pre-Dose (n=72, 74)    | 129 (± 83.5)   | 118 (± 41.4)   |  |  |
| Cycle 4 Day 1 Pre-Dose (n=69, 64)    | 153 (± 74.8)   | 155 (± 50.6)   |  |  |
| Cycle 8 Day 1 Pre-Dose (n=54, 51)    | 224 (± 126)  | 200 (± 100)  |  |  |
| Cycle 12 Day 1 Pre-Dose (n=31, 28)   | 223 (± 103)  | 210 (± 76.4)   |  |  |
| Cycle 16 Day 1 Pre-Dose (n=8, 6)     | 230 (± 71.6)   | 174 (± 64.9)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Prevalence of ADAs to Atezolizumab

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Prevalence of ADAs to Atezolizumab |
|-----------------|------------------------------------|

End point description:

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

End point timeframe:

Baseline

| End point values                  | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed       | 0 <sup>[3]</sup>                                     | 0 <sup>[4]</sup>                                     |  |  |
| Units: Percentage of participants |  |  |  |  |

Notes:

[3] - There is no data because the samples were not measured.

[4] - There is no data because the samples were not measured.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of ADAs to Atezolizumab

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Incidence of ADAs to Atezolizumab |
|-----------------|-----------------------------------|

End point description:

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

End point timeframe:

At pre-defined intervals from administration of study drug up to approximately 3-5 years

| End point values                  | Arm B:<br>Atezo+PBO+CisGem, followed<br>by Atezo+PBO | Arm A:<br>Atezo+Bev+CisGem, followed<br>by Atezo+Bev |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                                      | Reporting group                                      |  |  |
| Number of subjects analysed       | 0 <sup>[5]</sup>                                     | 0 <sup>[6]</sup>                                     |  |  |
| Units: Percentage of participants |  |  |  |  |

Notes:

[5] - There is no data because the samples were not measured.

[6] - There is no data because the samples were not measured.

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first study drug until the data cut-off on 16 May 2022 (up to approximately 14 months)

Adverse event reporting additional description:

Safety-evaluable population included all randomized participants who receive any amount of any component of protocol treatment.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Atezolizumab+Placebo+Cisplatin+Gemcitabine |
|-----------------------|--|

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

|                       |  |
|-----------------------|--|
| Reporting group title | Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine |
|-----------------------|--|

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

| Serious adverse events                            | Atezolizumab+Placebo+Cisplatin+Gemcitabine | Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine |  |
|---|--|--|--|
| Total subjects affected by serious adverse events |  |  |  |
| subjects affected / exposed                       | 42 / 81 (51.85%)                           | 36 / 78 (46.15%)                               |  |
| number of deaths (all causes)                     | 31   | 24   |  |
| number of deaths resulting from adverse events    | 1  | 1  |  |
| Vascular disorders                                |  |  |  |
| Hypotension                                       |  |  |  |
| subjects affected / exposed                       | 1 / 81 (1.23%)                             | 1 / 78 (1.28%)                                 |  |
| occurrences causally related to treatment / all   | 0 / 1                                      | 0 / 1  |  |
| deaths causally related to treatment / all        | 0 / 0                                      | 0 / 0  |  |
| Extremity necrosis                                |  |  |  |
| subjects affected / exposed                       | 1 / 81 (1.23%)                             | 0 / 78 (0.00%)                                 |  |
| occurrences causally related to treatment / all   | 0 / 1                                      | 0 / 0  |  |
| deaths causally related to treatment / all        | 0 / 0                                      | 0 / 0  |  |
| Hypertension                                      |  |  |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Thrombosis   |                |                |  |
| subjects affected / exposed                          | 2 / 81 (2.47%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Pyrexia  |                |                |  |
| subjects affected / exposed                          | 5 / 81 (6.17%) | 3 / 78 (3.85%) |  |
| occurrences causally related to treatment / all      | 1 / 10         | 2 / 5          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Oedema peripheral                                    |                |                |  |
| subjects affected / exposed                          | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Fatigue  |                |                |  |
| subjects affected / exposed                          | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Death  |                |                |  |
| subjects affected / exposed                          | 2 / 81 (2.47%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 2          | 0 / 1          |  |
| Asthenia   |                |                |  |
| subjects affected / exposed                          | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Reproductive system and breast disorders             |                |                |  |
| Prostatic obstruction                                |                |                |  |
| subjects affected / exposed                          | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Pleural effusion                                |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Epistaxis                                       |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dyspnoea  |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory failure                             |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary embolism                              |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 1 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonitis                                     |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Confusional state                               |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Investigations                                  |                |                |  |
| Alanine aminotransferase increased              |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Aspartate aminotransferase increased            |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood bilirubin increased                       |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood culture positive                          |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Platelet count decreased                        |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| White blood cell count decreased                |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Head injury                                     |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Spinal compression fracture                     |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Atrial fibrillation                             |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac failure acute                           |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac failure congestive                      |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| Cerebellar infarction                           |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Brain stem infarction                           |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cerebrovascular accident                        |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Subarachnoid haemorrhage                        |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Transient ischaemic attack                      |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| 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            |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Neutropenia                                     |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 3 / 3          | 3 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Febrile neutropenia                             |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Anaemia   |                |                |  |
| subjects affected / exposed                     | 6 / 81 (7.41%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 6 / 6          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Thrombocytopenia                                |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 3 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Abdominal pain                                  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Abdominal pain upper                            |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Colitis   |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Diarrhoea                                       |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Duodenal perforation                            |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Duodenal ulcer                                  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Enterocolitis                                   |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (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 / 81 (0.00%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal obstruction                    |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (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                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Intestinal perforation                          |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nausea  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Large intestinal stenosis                       |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pancreatitis                                    |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (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                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 1 / 1          |  |
| Hepatobiliary disorders                         |                |                |  |
| Biliary dilatation                              |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disease                           |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Jaundice  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Hepatitis                                       |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholestasis                                     |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholangitis                                     |                |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 4 / 81 (4.94%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 1 / 4          | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Biliary obstruction                             |                |                |  |
| subjects affected / exposed                     | 3 / 81 (3.70%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Jaundice cholestatic                            |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Nephropathy toxic                               |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute kidney injury                             |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 3 / 78 (3.85%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 3 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Back pain                                       |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 2 / 78 (2.56%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bone pain                                       |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gouty arthritis                                 |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Infections and infestations                     |                |                |  |
| Anal abscess                                    |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Appendicitis                                    |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bacteraemia                                     |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (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                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cystitis  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Diverticulitis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          |  |
| Enterocolitis infectious                        |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infection                                       |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Klebsiella sepsis                               |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Liver abscess                                   |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Urinary tract infection                         |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Septic shock                                    |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sepsis  |                |                |  |
| subjects affected / exposed                     | 3 / 81 (3.70%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 2 / 4          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Recurrent pyogenic cholangitis                  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia                                       |                |                |  |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Peritonitis                                     |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Hypokalaemia                                    |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypocalcaemia                                   |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypercalcaemia                                  |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Diabetes mellitus                               |                |                |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 78 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Decreased appetite                              |                |                |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 78 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Atezolizumab+Placebo+Cisplatin+Gemcitabine | Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events |  |  |  |
| subjects affected / exposed                           | 80 / 81 (98.77%)                           | 77 / 78 (98.72%)                               |  |
| Vascular disorders                                    |  |  |  |
| Hypertension  |  |  |  |
| subjects affected / exposed                           | 15 / 81 (18.52%)                           | 29 / 78 (37.18%)                               |  |
| occurrences (all)                                     | 16   | 35   |  |
| General disorders and administration site conditions  |  |  |  |
| Asthenia  |  |  |  |
| subjects affected / exposed                           | 16 / 81 (19.75%)                           | 14 / 78 (17.95%)                               |  |
| occurrences (all)                                     | 33   | 27   |  |
| Fatigue   |  |  |  |

|  |                        |                        |  |
|--|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 18 / 81 (22.22%)<br>22 | 20 / 78 (25.64%)<br>28 |  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)  | 7 / 81 (8.64%)<br>8    | 5 / 78 (6.41%)<br>5    |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 20 / 81 (24.69%)<br>41 | 13 / 78 (16.67%)<br>25 |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 8 / 81 (9.88%)<br>9    | 3 / 78 (3.85%)<br>3    |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 81 (1.23%)<br>2    | 10 / 78 (12.82%)<br>11 |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                        | 7 / 81 (8.64%)<br>7    | 1 / 78 (1.28%)<br>1    |  |
| Investigations<br>Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)             | 11 / 81 (13.58%)<br>13 | 6 / 78 (7.69%)<br>6    |  |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)                                | 7 / 81 (8.64%)<br>10   | 7 / 78 (8.97%)<br>7    |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)                     | 5 / 81 (6.17%)<br>7    | 4 / 78 (5.13%)<br>8    |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                     | 16 / 81 (19.75%)<br>19 | 7 / 78 (8.97%)<br>11   |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                       | 13 / 81 (16.05%)<br>20 | 9 / 78 (11.54%)<br>12  |  |
| C-reactive protein increased   |                        |                        |  |

|  |                        |                        |  |
|--|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                     | 5 / 81 (6.17%)<br>7    | 1 / 78 (1.28%)<br>1    |  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)       | 7 / 81 (8.64%)<br>17   | 7 / 78 (8.97%)<br>17   |  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)       | 32 / 81 (39.51%)<br>76 | 38 / 78 (48.72%)<br>93 |  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)         | 22 / 81 (27.16%)<br>47 | 22 / 78 (28.21%)<br>46 |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                 | 6 / 81 (7.41%)<br>6    | 9 / 78 (11.54%)<br>9   |  |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                 | 4 / 81 (4.94%)<br>4    | 5 / 78 (6.41%)<br>5    |  |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all) | 13 / 81 (16.05%)<br>33 | 15 / 78 (19.23%)<br>32 |  |
| Nervous system disorders   |                        |                        |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 81 (3.70%)<br>3    | 5 / 78 (6.41%)<br>5    |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                         | 5 / 81 (6.17%)<br>8    | 7 / 78 (8.97%)<br>7    |  |
| Blood and lymphatic system disorders   |                        |                        |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                      | 17 / 81 (20.99%)<br>31 | 17 / 78 (21.79%)<br>38 |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                          | 50 / 81 (61.73%)<br>77 | 38 / 78 (48.72%)<br>59 |  |
| Thrombocytopenia   |                        |                        |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all) | 6 / 81 (7.41%)<br>12 | 7 / 78 (8.97%)<br>18 |  |
| Gastrointestinal disorders                       |                      |                      |  |
| Ascites  |                      |                      |  |
| subjects affected / exposed                      | 5 / 81 (6.17%)       | 5 / 78 (6.41%)       |  |
| occurrences (all)                                | 5                    | 6                    |  |
| Abdominal pain                                   |                      |                      |  |
| subjects affected / exposed                      | 12 / 81 (14.81%)     | 13 / 78 (16.67%)     |  |
| occurrences (all)                                | 13                   | 14                   |  |
| Diarrhoea  |                      |                      |  |
| subjects affected / exposed                      | 11 / 81 (13.58%)     | 13 / 78 (16.67%)     |  |
| occurrences (all)                                | 12                   | 21                   |  |
| Constipation                                     |                      |                      |  |
| subjects affected / exposed                      | 21 / 81 (25.93%)     | 27 / 78 (34.62%)     |  |
| occurrences (all)                                | 23                   | 35                   |  |
| Stomatitis                                       |                      |                      |  |
| subjects affected / exposed                      | 4 / 81 (4.94%)       | 7 / 78 (8.97%)       |  |
| occurrences (all)                                | 4                    | 7                    |  |
| Nausea   |                      |                      |  |
| subjects affected / exposed                      | 32 / 81 (39.51%)     | 32 / 78 (41.03%)     |  |
| occurrences (all)                                | 43                   | 50                   |  |
| Haemorrhoids                                     |                      |                      |  |
| subjects affected / exposed                      | 0 / 81 (0.00%)       | 4 / 78 (5.13%)       |  |
| occurrences (all)                                | 0                    | 4                    |  |
| Dyspepsia  |                      |                      |  |
| subjects affected / exposed                      | 7 / 81 (8.64%)       | 2 / 78 (2.56%)       |  |
| occurrences (all)                                | 7                    | 2                    |  |
| Vomiting   |                      |                      |  |
| subjects affected / exposed                      | 11 / 81 (13.58%)     | 15 / 78 (19.23%)     |  |
| occurrences (all)                                | 11                   | 22                   |  |
| Skin and subcutaneous tissue disorders           |                      |                      |  |
| Alopecia   |                      |                      |  |
| subjects affected / exposed                      | 2 / 81 (2.47%)       | 4 / 78 (5.13%)       |  |
| occurrences (all)                                | 2                    | 4                    |  |
| Pruritus   |                      |                      |  |

|   |                        |                        |  |
|---|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 6 / 81 (7.41%)<br>7    | 6 / 78 (7.69%)<br>8    |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 8 / 81 (9.88%)<br>8    | 10 / 78 (12.82%)<br>14 |  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)   | 1 / 81 (1.23%)<br>1    | 4 / 78 (5.13%)<br>4    |  |
| Renal and urinary disorders<br>Proteinuria<br>subjects affected / exposed<br>occurrences (all)                    | 8 / 81 (9.88%)<br>8    | 13 / 78 (16.67%)<br>15 |  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                         | 5 / 81 (6.17%)<br>5    | 4 / 78 (5.13%)<br>4    |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 4 / 81 (4.94%)<br>5    | 7 / 78 (8.97%)<br>8    |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 5 / 81 (6.17%)<br>5    | 6 / 78 (7.69%)<br>10   |  |
| Infections and infestations<br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)        | 5 / 81 (6.17%)<br>5    | 4 / 78 (5.13%)<br>4    |  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)  | 9 / 81 (11.11%)<br>9   | 8 / 78 (10.26%)<br>8   |  |
| Metabolism and nutrition disorders<br>Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)           | 11 / 81 (13.58%)<br>12 | 7 / 78 (8.97%)<br>10   |  |
| Decreased appetite  |                        |                        |  |



|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 14 / 81 (17.28%) | 15 / 78 (19.23%) |  |
| occurrences (all)           | 15               | 16               |  |
| Hyperglycaemia              |                  |                  |  |
| subjects affected / exposed | 5 / 81 (6.17%)   | 1 / 78 (1.28%)   |  |
| occurrences (all)           | 5                | 1                |  |
| Hypoalbuminaemia            |                  |                  |  |
| subjects affected / exposed | 6 / 81 (7.41%)   | 8 / 78 (10.26%)  |  |
| occurrences (all)           | 6                | 8                |  |
| Hypokalaemia                |                  |                  |  |
| subjects affected / exposed | 11 / 81 (13.58%) | 6 / 78 (7.69%)   |  |
| occurrences (all)           | 12               | 7                |  |
| Hypomagnesaemia             |                  |                  |  |
| subjects affected / exposed | 6 / 81 (7.41%)   | 10 / 78 (12.82%) |  |
| occurrences (all)           | 6                | 12               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 07 October 2020   | Protocol has been amended to include sensitivity analysis to assess the robustness of the primary progression-free survival analysis. A sensitivity analysis will be performed by incorporating an additional censoring rule for participants who take new anti-cancer therapy prior to occurrence of radiographic progression. These participants will be censored at the last tumor assessment before the start of the new treatment, regardless of progression or death afterwards.  |
| 03 March 2021     | Protocol has been amended to include updates to the exclusion criteria around symptomatic and asymptomatic brain metastasis. Also, participants with large centrally located pulmonary metastases; clear tumor infiltration into the thoracic great vessels seen on imaging; and clear cavitation of pulmonary lesions seen on imaging will be excluded from this study. The order of administration of cisplatin and gemcitabine has been clarified. The list of identified risks for atezolizumab have been revised to include severe cutaneous adverse reactions. Language has been added to clarify that hemophagocytic lymphohistiocytosis and macrophage activation syndrome are considered potential risks for atezolizumab. |
| 27 September 2022 | Protocol has been amended to add a final overall survival analysis. The timing of the patient-reported outcome assessments has been clarified.  |
| 03 February 2023  | Protocol has been amended to include pericardial disorders, myelitis, and facial paresis in the list of identified risks for atezolizumab. Hemophagocytic lymphohistiocytosis has been updated from a potential risk to an identified risk associated with atezolizumab.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported