



## Clinical trial results:

### A Phase III, Double-blind, Placebo-controlled, Randomized Study of Ipatasertib in Combination with Atezolizumab and Paclitaxel as a Treatment for Patients with Locally Advanced Unresectable or Metastatic Triple-Negative Breast Cancer

#### Summary

|                          |                                              |
|--------------------------|----------------------------------------------|
| EudraCT number           | 2019-000810-12                               |
| Trial protocol           | CZ FR AT PL PT IE ES FI HU BE GR BG DK RO IT |
| Global end of trial date | 28 February 2023                             |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 13 March 2024 |
| First version publication date | 13 March 2024 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | CO41101 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04177108 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                        |
|------------------------------|--------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | F. Hoffmann-La Roche AG                                                                                |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, 4070                                                        |
| Public contact               | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, CH +41 616878333, global.trial_information@roche.com |
| Scientific contact           | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, CH +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                                       | Final            |
| Date of interim/final analysis                       | 28 February 2023 |
| Is this the analysis of the primary completion data? | No               |

|                                  |                  |
|----------------------------------|------------------|
| Global end of trial reached?     | Yes              |
| Global end of trial date         | 28 February 2023 |
| Was the trial ended prematurely? | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy and safety of ipatasertib in combination with atezolizumab and paclitaxel in locally advanced or metastatic Triple-Negative Breast Cancer (TNBC) previously untreated in this setting.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 25 November 2019 |
| 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 | Argentina: 13     |
| Country: Number of subjects enrolled | Australia: 18     |
| Country: Number of subjects enrolled | Austria: 1        |
| Country: Number of subjects enrolled | Belgium: 1        |
| Country: Number of subjects enrolled | Bulgaria: 1       |
| Country: Number of subjects enrolled | Brazil: 2         |
| Country: Number of subjects enrolled | Canada: 1         |
| Country: Number of subjects enrolled | Switzerland: 1    |
| Country: Number of subjects enrolled | Colombia: 3       |
| Country: Number of subjects enrolled | Costa Rica: 3     |
| Country: Number of subjects enrolled | Czechia: 2        |
| Country: Number of subjects enrolled | Denmark: 2        |
| Country: Number of subjects enrolled | Spain: 27         |
| Country: Number of subjects enrolled | Finland: 2        |
| Country: Number of subjects enrolled | France: 1         |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Hong Kong: 5      |
| Country: Number of subjects enrolled | India: 1          |
| Country: Number of subjects enrolled | Israel: 1         |
| Country: Number of subjects enrolled | Italy: 18         |
| Country: Number of subjects enrolled | Japan: 6          |

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 28 |
| Country: Number of subjects enrolled | Mexico: 16             |
| Country: Number of subjects enrolled | Peru: 12               |
| Country: Number of subjects enrolled | Poland: 12             |
| Country: Number of subjects enrolled | Portugal: 2            |
| Country: Number of subjects enrolled | Romania: 2             |
| Country: Number of subjects enrolled | Russian Federation: 8  |
| Country: Number of subjects enrolled | Thailand: 10           |
| Country: Number of subjects enrolled | Türkiye: 9             |
| Country: Number of subjects enrolled | Taiwan: 9              |
| Country: Number of subjects enrolled | Ukraine: 13            |
| Country: Number of subjects enrolled | United States: 8       |
| Worldwide total number of subjects   | 242                    |
| EEA total number of subjects         | 71                     |

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)                      | 201 |
| From 65 to 84 years                       | 41  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 215 investigative centers from 25 November 2019 to 28 February 2023.

### Pre-assignment

Screening details:

A total of 242 participants with Advanced TNBC were enrolled, of which 127 participants were randomised to cohort 1 {programmed death-ligand 1 (PD-L1) Non-positive} and 115 participants to cohort 2 (PD-L1 positive).

### 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, Monitor, Carer, Data analyst, Assessor |

### Arms

|                              |                                                         |
|------------------------------|---------------------------------------------------------|
| Are arms mutually exclusive? | Yes                                                     |
| <b>Arm title</b>             | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |

Arm description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 milligrams per meter square (mg/m<sup>2</sup>), intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, orally (PO), once daily (QD), from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Ipatasertib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Ipatasertib will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Paclitaxel will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Atezolizumab will be administered as per the dosage regimen mentioned in arm descriptions.

|                  |                                                    |
|------------------|----------------------------------------------------|
| <b>Arm title</b> | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel |
|------------------|----------------------------------------------------|

Arm description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion

on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Ipatasertib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Ipatasertib will be administered as per the dosage regimen mentioned in arm descriptions.

|                                        |                               |
|----------------------------------------|-------------------------------|
| Investigational medicinal product name | Atezolizumab_matching placebo |
| Investigational medicinal product code |                               |
| Other name                             |                               |
| Pharmaceutical forms                   | Solution for infusion         |
| Routes of administration               | Intravenous use               |

Dosage and administration details:

Atezolizumab matching placebo will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Paclitaxel will be administered as per the dosage regimen mentioned in arm descriptions.

|                  |                                                |
|------------------|------------------------------------------------|
| <b>Arm title</b> | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel |
|------------------|------------------------------------------------|

Arm description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                                        |                              |
|----------------------------------------|------------------------------|
| Arm type                               | Experimental                 |
| Investigational medicinal product name | Ipatasertib_matching placebo |
| Investigational medicinal product code |                              |
| Other name                             |                              |
| Pharmaceutical forms                   | Tablet                       |
| Routes of administration               | Oral use                     |

Dosage and administration details:

Ipatasertib matching placebo will be administered as per the dosage regimen mentioned in arm descriptions.

|                                        |                               |
|----------------------------------------|-------------------------------|
| Investigational medicinal product name | Atezolizumab_matching placebo |
| Investigational medicinal product code |                               |
| Other name                             |                               |
| Pharmaceutical forms                   | Solution for infusion         |
| Routes of administration               | Intravenous use               |

Dosage and administration details:

Atezolizumab matching placebo will be administered as per the dosage regimen mentioned in arm descriptions.

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code |            |
| Other name                             |            |

|                          |                       |
|--------------------------|-----------------------|
| Pharmaceutical forms     | Solution for infusion |
| Routes of administration | Intravenous use       |

Dosage and administration details:

Paclitaxel will be administered as per the dosage regimen mentioned in arm descriptions.

|                  |                                                         |
|------------------|---------------------------------------------------------|
| <b>Arm title</b> | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|------------------|---------------------------------------------------------|

Arm description:

TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Ipatasertib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Ipatasertib will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Paclitaxel will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Atezolizumab will be administered as per the dosage regimen mentioned in arm descriptions.

|                  |                                                    |
|------------------|----------------------------------------------------|
| <b>Arm title</b> | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |
|------------------|----------------------------------------------------|

Arm description:

TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                                        |                              |
|----------------------------------------|------------------------------|
| Arm type                               | Experimental                 |
| Investigational medicinal product name | Ipatasertib_matching placebo |
| Investigational medicinal product code |                              |
| Other name                             |                              |
| Pharmaceutical forms                   | Tablet                       |
| Routes of administration               | Oral use                     |

Dosage and administration details:

Ipatasertib matching placebo will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Atezolizumab will be administered as per the dosage regimen mentioned in arm descriptions.

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

Dosage and administration details:

Paclitaxel will be administered as per the dosage regimen mentioned in arm descriptions.

| <b>Number of subjects in period 1</b> | Cohort 1 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 1 Arm B:<br>Ipatasertib +<br>Placebo + Paclitaxel | Cohort 1 Arm C:<br>Placebo + Placebo +<br>Paclitaxel |
|---------------------------------------|------------------------------------------------------------------|----------------------------------------------------------|------------------------------------------------------|
| Started                               | 43                                                               | 43                                                       | 41                                                   |
| Completed                             | 0                                                                | 0                                                        | 0                                                    |
| Not completed                         | 43                                                               | 43                                                       | 41                                                   |
| Adverse event, serious fatal          | 16                                                               | 19                                                       | 13                                                   |
| Consent withdrawn by subject          | 4                                                                | 8                                                        | 9                                                    |
| Physician decision                    | 23                                                               | 15                                                       | 18                                                   |
| Reason Not Specified                  | -                                                                | 1                                                        | -                                                    |
| Lost to follow-up                     | -                                                                | -                                                        | 1                                                    |

| <b>Number of subjects in period 1</b> | Cohort 2 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 2 Arm B:<br>Placebo+<br>Atezolizumab +<br>Paclitaxel |
|---------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------|
| Started                               | 58                                                               | 57                                                          |
| Completed                             | 0                                                                | 0                                                           |
| Not completed                         | 58                                                               | 57                                                          |
| Adverse event, serious fatal          | 17                                                               | 18                                                          |
| Consent withdrawn by subject          | 11                                                               | 13                                                          |
| Physician decision                    | 29                                                               | 23                                                          |
| Reason Not Specified                  | -                                                                | 2                                                           |
| Lost to follow-up                     | 1                                                                | 1                                                           |

## Baseline characteristics

### Reporting groups

|                       |                                                         |
|-----------------------|---------------------------------------------------------|
| Reporting group title | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|-----------------------|---------------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 milligrams per meter square (mg/m<sup>2</sup>), intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, orally (PO), once daily (QD), from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                    |
|-----------------------|----------------------------------------------------|
| Reporting group title | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel |
|-----------------------|----------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                |
|-----------------------|------------------------------------------------|
| Reporting group title | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel |
|-----------------------|------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                         |
|-----------------------|---------------------------------------------------------|
| Reporting group title | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|-----------------------|---------------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                    |
|-----------------------|----------------------------------------------------|
| Reporting group title | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |
|-----------------------|----------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

| Reporting group values                 | Cohort 1 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 1 Arm B:<br>Ipatasertib +<br>Placebo + Paclitaxel | Cohort 1 Arm C:<br>Placebo + Placebo +<br>Paclitaxel |
|----------------------------------------|------------------------------------------------------------------|----------------------------------------------------------|------------------------------------------------------|
| Number of subjects                     | 43                                                               | 43                                                       | 41                                                   |
| Age categorical<br>Units: participants |                                                                  |                                                          |                                                      |

|                                                                         |                |                |                |
|-------------------------------------------------------------------------|----------------|----------------|----------------|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 55.5<br>± 11.7 | 50.8<br>± 11.6 | 53.5<br>± 10.7 |
| Sex/Gender, Customized<br>Units: participants<br>Female                 | 43             | 43             | 41             |
| Race (NIH/OMB)<br>Units: Subjects<br>American Indian or Alaska Native   | 5              | 3              | 1              |

|                                           |    |    |    |
|-------------------------------------------|----|----|----|
| Asian                                     | 10 | 7  | 9  |
| Native Hawaiian or Other Pacific Islander | 0  | 0  | 0  |
| Black or African American                 | 2  | 2  | 0  |
| White                                     | 26 | 29 | 29 |
| More than one race                        | 0  | 0  | 1  |
| Unknown or Not Reported                   | 0  | 2  | 1  |
| Ethnicity (NIH/OMB)                       |    |    |    |
| Units: Subjects                           |    |    |    |
| Hispanic or Latino                        | 8  | 9  | 6  |
| Not Hispanic or Latino                    | 32 | 32 | 35 |
| Unknown or Not Reported                   | 3  | 2  | 0  |

| Reporting group values | Cohort 2 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 2 Arm B:<br>Placebo+<br>Atezolizumab +<br>Paclitaxel | Total |
|------------------------|------------------------------------------------------------------|-------------------------------------------------------------|-------|
| Number of subjects     | 58                                                               | 57                                                          | 242   |
| Age categorical        |                                                                  |                                                             |       |
| Units: participants    |                                                                  |                                                             |       |

|                        |        |        |     |
|------------------------|--------|--------|-----|
| Age Continuous         |        |        |     |
| Units: years           |        |        |     |
| arithmetic mean        | 53.7   | 51.1   |     |
| standard deviation     | ± 12.1 | ± 11.7 | -   |
| Sex/Gender, Customized |        |        |     |
| Units: participants    |        |        |     |
| Female                 | 58     | 57     | 242 |

|                                           |    |    |     |
|-------------------------------------------|----|----|-----|
| Race (NIH/OMB)                            |    |    |     |
| Units: Subjects                           |    |    |     |
| American Indian or Alaska Native          | 5  | 6  | 20  |
| Asian                                     | 19 | 16 | 61  |
| Native Hawaiian or Other Pacific Islander | 0  | 0  | 0   |
| Black or African American                 | 2  | 2  | 8   |
| White                                     | 29 | 32 | 145 |
| More than one race                        | 0  | 1  | 2   |
| Unknown or Not Reported                   | 3  | 0  | 6   |
| Ethnicity (NIH/OMB)                       |    |    |     |
| Units: Subjects                           |    |    |     |
| Hispanic or Latino                        | 15 | 14 | 52  |
| Not Hispanic or Latino                    | 41 | 43 | 183 |
| Unknown or Not Reported                   | 2  | 0  | 7   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
| Reporting group description:<br>TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 milligrams per meter square (mg/m <sup>2</sup> ), intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, orally (PO), once daily (QD), from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first. |                                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel      |
| Reporting group description:<br>TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m <sup>2</sup> , IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.                                                          |                                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel          |
| Reporting group description:<br>TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m <sup>2</sup> , IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.                                                 |                                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
| Reporting group description:<br>TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m <sup>2</sup> , IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.                                                                       |                                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel      |
| Reporting group description:<br>TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m <sup>2</sup> , IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.                                                              |                                                         |

### Primary: Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1

|                                                                                                                                                                                                                                                                                                                |                                                                                                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                | Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 |
| End point description:<br>PFS was defined as the time from randomization to the first occurrence of disease progression as determined locally by RECIST or death from any cause during treatment, whichever occurs first. Intent-to-Treat (ITT) population included all participants randomised in this study. |                                                                                                                |
| End point type                                                                                                                                                                                                                                                                                                 | Primary                                                                                                        |
| End point timeframe:<br>From Randomisation to disease progression, study completion, or death (up to 39 months)                                                                                                                                                                                                |                                                                                                                |

| <b>End point values</b>          | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|----------------------------------|---------------------------------------------------------|----------------------------------------------------|------------------------------------------------|---------------------------------------------------------|
| Subject group type               | Reporting group                                         | Reporting group                                    | Reporting group                                | Reporting group                                         |
| Number of subjects analysed      | 43                                                      | 43                                                 | 41                                             | 58                                                      |
| Units: months                    |                                                         |                                                    |                                                |                                                         |
| median (confidence interval 95%) | 7.1 (5.1 to 9.3)                                        | 5.6 (3.7 to 8.2)                                   | 3.7 (3.6 to 5.4)                               | 5.6 (5.4 to 9.2)                                        |

| <b>End point values</b>          | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |  |  |  |
|----------------------------------|----------------------------------------------------|--|--|--|
| Subject group type               | Reporting group                                    |  |  |  |
| Number of subjects analysed      | 57                                                 |  |  |  |
| Units: months                    |                                                    |  |  |  |
| median (confidence interval 95%) | 5.7 (4.0 to 9.1)                                   |  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>       | Cohort 1 Arm A Versus Cohort 1 Arm C                                                                     |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel v Cohort 1 Arm C: Placebo + Placebo + Paclitaxel |
| Number of subjects included in analysis | 84                                                                                                       |
| Analysis specification                  | Pre-specified                                                                                            |
| Analysis type                           | superiority                                                                                              |
| P-value                                 | = 0.0098                                                                                                 |
| Method                                  | Logrank                                                                                                  |
| Parameter estimate                      | Hazard ratio (HR)                                                                                        |
| Point estimate                          | 0.49                                                                                                     |
| Confidence interval                     |                                                                                                          |
| level                                   | 95 %                                                                                                     |
| sides                                   | 2-sided                                                                                                  |
| lower limit                             | 0.28                                                                                                     |
| upper limit                             | 0.85                                                                                                     |

| <b>Statistical analysis title</b>       | Cohort 2 Arm A Versus Cohort 2 Arm B                                                                         |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel v Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |
| Number of subjects included in analysis | 115                                                                                                          |
| Analysis specification                  | Pre-specified                                                                                                |
| Analysis type                           | superiority                                                                                                  |
| P-value                                 | = 0.9809                                                                                                     |
| Method                                  | Logrank                                                                                                      |
| Parameter estimate                      | Hazard ratio (HR)                                                                                            |
| Point estimate                          | 0.99                                                                                                         |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.63    |
| upper limit         | 1.58    |

|                                         |                                                                                                     |
|-----------------------------------------|-----------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Cohort 1 Arm B Versus Cohort 1 Arm C                                                                |
| Comparison groups                       | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel v Cohort 1 Arm C: Placebo + Placebo + Paclitaxel |
| Number of subjects included in analysis | 84                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                       |
| Analysis type                           | superiority                                                                                         |
| P-value                                 | = 0.2396                                                                                            |
| Method                                  | Logrank                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                   |
| Point estimate                          | 0.72                                                                                                |
| Confidence interval                     |                                                                                                     |
| level                                   | 95 %                                                                                                |
| sides                                   | 2-sided                                                                                             |
| lower limit                             | 0.42                                                                                                |
| upper limit                             | 1.25                                                                                                |

### Primary: Overall Survival (OS)

|                                                                                                                                                                                                                                                                                                                                  |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| End point title                                                                                                                                                                                                                                                                                                                  | Overall Survival (OS) |
| End point description:                                                                                                                                                                                                                                                                                                           |                       |
| OS was defined as the time from randomisation to the time of death from any cause on study. Here, 99999 indicates that median and upper limit of 95% confidence interval (CI) could not be calculated due to insufficient number of participants with events. ITT population included all participants randomised in this study. |                       |
| End point type                                                                                                                                                                                                                                                                                                                   | Primary               |
| End point timeframe:                                                                                                                                                                                                                                                                                                             |                       |
| From randomization up to study completion or death (Up to 39 months)                                                                                                                                                                                                                                                             |                       |

| End point values                 | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|----------------------------------|---------------------------------------------------------|----------------------------------------------------|------------------------------------------------|---------------------------------------------------------|
| Subject group type               | Reporting group                                         | Reporting group                                    | Reporting group                                | Reporting group                                         |
| Number of subjects analysed      | 43                                                      | 43                                                 | 41                                             | 58                                                      |
| Units: months                    |                                                         |                                                    |                                                |                                                         |
| median (confidence interval 95%) | 15.7 (12.5 to 99999)                                    | 15.3 (15.3 to 99999)                               | 16.6 (9.6 to 99999)                            | 99999 (14.1 to 99999)                                   |

|                                  |                                                    |  |  |  |
|----------------------------------|----------------------------------------------------|--|--|--|
| <b>End point values</b>          | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |  |  |  |
| Subject group type               | Reporting group                                    |  |  |  |
| Number of subjects analysed      | 57                                                 |  |  |  |
| Units: months                    |                                                    |  |  |  |
| median (confidence interval 95%) | 17.2 (13.4 to 99999)                               |  |  |  |

## Statistical analyses

|                                         |                                                                                                          |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Cohort 1 Arm A Versus Cohort 1 Arm C                                                                     |
| Comparison groups                       | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel v Cohort 1 Arm C: Placebo + Placebo + Paclitaxel |
| Number of subjects included in analysis | 84                                                                                                       |
| Analysis specification                  | Pre-specified                                                                                            |
| Analysis type                           | superiority                                                                                              |
| P-value                                 | = 0.6805                                                                                                 |
| Method                                  | Logrank                                                                                                  |
| Parameter estimate                      | Hazard ratio (HR)                                                                                        |
| Point estimate                          | 1.17                                                                                                     |
| Confidence interval                     |                                                                                                          |
| level                                   | 95 %                                                                                                     |
| sides                                   | 2-sided                                                                                                  |
| lower limit                             | 0.55                                                                                                     |
| upper limit                             | 2.51                                                                                                     |

|                                         |                                                                                                              |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Cohort 2 Arm A Versus Cohort 2 Arm B                                                                         |
| Comparison groups                       | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel v Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |
| Number of subjects included in analysis | 115                                                                                                          |
| Analysis specification                  | Pre-specified                                                                                                |
| Analysis type                           | superiority                                                                                                  |
| P-value                                 | = 0.9164                                                                                                     |
| Method                                  | Logrank                                                                                                      |
| Parameter estimate                      | Hazard ratio (HR)                                                                                            |
| Point estimate                          | 1.04                                                                                                         |
| Confidence interval                     |                                                                                                              |
| level                                   | 95 %                                                                                                         |
| sides                                   | 2-sided                                                                                                      |
| lower limit                             | 0.52                                                                                                         |
| upper limit                             | 2.06                                                                                                         |

|                                   |                                                               |
|-----------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b> | Cohort 1 Arm B Versus Cohort 1 Arm C                          |
| Comparison groups                 | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel v Cohort 1 |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
|                                         | Arm C: Placebo + Placebo + Paclitaxel |
| Number of subjects included in analysis | 84                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.6314                              |
| Method                                  | Logrank                               |
| Parameter estimate                      | Hazard ratio (HR)                     |
| Point estimate                          | 1.21                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 0.55                                  |
| upper limit                             | 2.64                                  |

### Secondary: Number of Participants with Adverse Events (AEs)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Number of Participants with Adverse Events (AEs) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                  |
| An AE is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Safety-evaluable population included all randomised participants who took at least one dose of the study treatment. |                                                  |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Secondary                                        |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                  |
| Up to 39 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                  |

| End point values            | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|-----------------------------|---------------------------------------------------------|----------------------------------------------------|------------------------------------------------|---------------------------------------------------------|
| Subject group type          | Reporting group                                         | Reporting group                                    | Reporting group                                | Reporting group                                         |
| Number of subjects analysed | 43                                                      | 43                                                 | 41                                             | 58                                                      |
| Units: participants         | 42                                                      | 43                                                 | 40                                             | 58                                                      |

| End point values            | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |  |  |  |
|-----------------------------|----------------------------------------------------|--|--|--|
| Subject group type          | Reporting group                                    |  |  |  |
| Number of subjects analysed | 57                                                 |  |  |  |
| Units: participants         | 56                                                 |  |  |  |

### Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 39 months

Adverse event reporting additional description:

Safety-evaluable population included all randomized participants who took at least one dose of the study treatment.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 18 |
|--------------------|----|

### Reporting groups

|                       |                                                         |
|-----------------------|---------------------------------------------------------|
| Reporting group title | Cohort 1 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|-----------------------|---------------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 milligrams per meter square (mg/m<sup>2</sup>), intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, orally (PO), once daily (QD), from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                    |
|-----------------------|----------------------------------------------------|
| Reporting group title | Cohort 1 Arm B: Ipatasertib + Placebo + Paclitaxel |
|-----------------------|----------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                    |
|-----------------------|----------------------------------------------------|
| Reporting group title | Cohort 2 Arm B: Placebo+ Atezolizumab + Paclitaxel |
|-----------------------|----------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                         |
|-----------------------|---------------------------------------------------------|
| Reporting group title | Cohort 2 Arm A: Ipatasertib + Atezolizumab + Paclitaxel |
|-----------------------|---------------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib, 400 mg, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab, 840 mg, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

|                       |                                                |
|-----------------------|------------------------------------------------|
| Reporting group title | Cohort 1 Arm C: Placebo + Placebo + Paclitaxel |
|-----------------------|------------------------------------------------|

Reporting group description:

TNBC participants with PD-L1 non-positive received a combination of paclitaxel, 80 mg/m<sup>2</sup>, IV infusion on Days 1, 8, and 15 of each 28-day cycle and ipatasertib-matching placebo, PO, QD, from Day 1 to Day 21 of each 28-day cycle and atezolizumab-matching placebo, IV infusion on Day 1 and 15 of each 28-day cycle until loss of clinical benefit, unacceptable toxicity, or withdrawal of consent, whichever occurred first.

| Serious adverse events                            | Cohort 1 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 1 Arm B:<br>Ipatasertib +<br>Placebo + Paclitaxel | Cohort 2 Arm B:<br>Placebo+<br>Atezolizumab +<br>Paclitaxel |
|---------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|
| Total subjects affected by serious adverse events |                                                                  |                                                          |                                                             |
| subjects affected / exposed                       | 14 / 43 (32.56%)                                                 | 7 / 43 (16.28%)                                          | 9 / 57 (15.79%)                                             |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| number of deaths (all causes)                        | 16             | 19             | 18             |
| number of deaths resulting from adverse events       | 3              | 0              | 0              |
| Vascular disorders                                   |                |                |                |
| Hypotension                                          |                |                |                |
| subjects affected / exposed                          | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Pyrexia                                              |                |                |                |
| subjects affected / exposed                          | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Death                                                |                |                |                |
| subjects affected / exposed                          | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 1          | 0 / 0          |
| Fatigue                                              |                |                |                |
| subjects affected / exposed                          | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Immune system disorders                              |                |                |                |
| Hypersensitivity                                     |                |                |                |
| subjects affected / exposed                          | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders      |                |                |                |
| Pleural effusion                                     |                |                |                |
| subjects affected / exposed                          | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                                   |                |                |                |
| subjects affected / exposed                          | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Pneumonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vocal cord atrophy                              |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Alanine aminotransferase increased              |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Aspartate aminotransferase increased            |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Pelvic fracture                                 |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infusion related reaction                       |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Radius fracture                                 |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Cardiac arrest                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Facial paralysis                                |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Transient ischaemic attack                      |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vocal cord paresis                              |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neutropenia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 2 / 43 (4.65%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 4 / 4          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                                                        |                |                |                |
|----------------------------------------------------------------------------------------|----------------|----------------|----------------|
| Upper gastrointestinal haemorrhage<br>subjects affected / exposed                      | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal pain<br>subjects affected / exposed                                          | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal toxicity<br>subjects affected / exposed                               | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders<br>Drug eruption<br>subjects affected / exposed | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Eczema<br>subjects affected / exposed                                                  | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Rash<br>subjects affected / exposed                                                    | 3 / 43 (6.98%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 3 / 3          | 1 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Urticaria<br>subjects affected / exposed                                               | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders<br>Acute kidney injury<br>subjects affected / exposed      | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                                          | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neck pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Myositis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lymphangitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clostridium difficile colitis                   |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia viral                                 |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Upper respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Cholecystitis infective                         |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diarrhoea infectious                            |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 2 / 43 (4.65%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Septic shock                                    |                |                |                |
| subjects affected / exposed                     | 2 / 43 (4.65%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 2 / 2          | 0 / 0          | 0 / 0          |
| Escherichia infection                           |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Device related infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis acute                            |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lung abscess                                    |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| COVID-19                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clostridium colitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sepsis                                          |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| COVID-19 pneumonia                              |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infection                                       |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular device infection                       |                |                |                |
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Staphylococcal infection                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyperglycaemia                                  |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 43 (2.33%) | 0 / 43 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                        | Cohort 2 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 1 Arm C:<br>Placebo + Placebo +<br>Paclitaxel |  |
|------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------|--|
| Total subjects affected by serious adverse events    |                                                                  |                                                      |  |
| subjects affected / exposed                          | 16 / 58 (27.59%)                                                 | 7 / 41 (17.07%)                                      |  |
| number of deaths (all causes)                        | 18                                                               | 13                                                   |  |
| number of deaths resulting from adverse events       | 0                                                                | 1                                                    |  |
| Vascular disorders                                   |                                                                  |                                                      |  |
| Hypotension                                          |                                                                  |                                                      |  |
| subjects affected / exposed                          | 0 / 58 (0.00%)                                                   | 0 / 41 (0.00%)                                       |  |
| occurrences causally related to treatment / all      | 0 / 0                                                            | 0 / 0                                                |  |
| deaths causally related to treatment / all           | 0 / 0                                                            | 0 / 0                                                |  |
| General disorders and administration site conditions |                                                                  |                                                      |  |
| Pyrexia                                              |                                                                  |                                                      |  |
| subjects affected / exposed                          | 1 / 58 (1.72%)                                                   | 0 / 41 (0.00%)                                       |  |
| occurrences causally related to treatment / all      | 2 / 2                                                            | 0 / 0                                                |  |
| deaths causally related to treatment / all           | 0 / 0                                                            | 0 / 0                                                |  |
| Death                                                |                                                                  |                                                      |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Fatigue                                         |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Immune system disorders                         |                |                |  |
| Hypersensitivity                                |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Pleural effusion                                |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 1 / 41 (2.44%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary embolism                              |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonitis                                     |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vocal cord atrophy                              |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Investigations                                  |                |                |  |
| Alanine aminotransferase increased              |                |                |  |
| subjects affected / exposed                     | 2 / 58 (3.45%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Aspartate aminotransferase increased            |                |                |  |
| subjects affected / exposed                     | 2 / 58 (3.45%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Pelvic fracture                                 |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infusion related reaction                       |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Radius fracture                                 |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Cardiac arrest                                  |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (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                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| Facial paralysis                                |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Transient ischaemic attack                      |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vocal cord paresis                              |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood and lymphatic system disorders            |                |                |  |
| Anaemia                                         |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutropenia                                     |                |                |  |
| subjects affected / exposed                     | 2 / 58 (3.45%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Diarrhoea                                       |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Upper gastrointestinal haemorrhage              |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Abdominal pain                                  |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal toxicity                       |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (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          |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Drug eruption                                   |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eczema                                          |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Rash                                            |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Urticaria                                       |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Acute kidney injury                             |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Back pain                                       |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neck pain                                       |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Myositis                                        |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 1 / 41 (2.44%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 1 / 1          |  |

|                                                                                                                                                                          |                                  |                                  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|----------------------------------|--|
| Infections and infestations<br>Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 41 (2.44%)<br>0 / 1<br>0 / 0 |  |
| Lymphangitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 41 (2.44%)<br>0 / 1<br>0 / 0 |  |
| Clostridium difficile colitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all            | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 41 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Pneumonia viral<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                          | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 41 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all        | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 41 (2.44%)<br>0 / 1<br>0 / 0 |  |
| Cholecystitis infective<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                  | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 41 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Diarrhoea infectious<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                     | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 41 (2.44%)<br>0 / 1<br>0 / 0 |  |
| Cellulitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                               | 0 / 58 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 41 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Septic shock                                                                                                                                                             |                                  |                                  |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Escherichia infection                           |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device related infection                        |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pyelonephritis acute                            |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 1 / 41 (2.44%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Lung abscess                                    |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| COVID-19                                        |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 2 / 41 (4.88%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Clostridium colitis                             |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 1 / 41 (2.44%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sepsis                                          |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| COVID-19 pneumonia                              |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pyelonephritis                                  |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Urinary tract infection                         |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infection                                       |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vascular device infection                       |                |                |  |
| subjects affected / exposed                     | 1 / 58 (1.72%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Staphylococcal infection                        |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Dehydration                                     |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyperglycaemia                                  |                |                |  |
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyponatraemia                                   |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 58 (0.00%) | 0 / 41 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| 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>                     | Cohort 1 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 1 Arm B:<br>Ipatasertib +<br>Placebo + Paclitaxel | Cohort 2 Arm B:<br>Placebo+<br>Atezolizumab +<br>Paclitaxel |
|-------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|
| Total subjects affected by non-serious adverse events |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 42 / 43 (97.67%)                                                 | 42 / 43 (97.67%)                                         | 55 / 57 (96.49%)                                            |
| Vascular disorders                                    |                                                                  |                                                          |                                                             |
| Lymphoedema                                           |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 3 / 43 (6.98%)                                                   | 1 / 43 (2.33%)                                           | 1 / 57 (1.75%)                                              |
| occurrences (all)                                     | 3                                                                | 1                                                        | 1                                                           |
| Hypertension                                          |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 0 / 43 (0.00%)                                                   | 1 / 43 (2.33%)                                           | 1 / 57 (1.75%)                                              |
| occurrences (all)                                     | 0                                                                | 1                                                        | 1                                                           |
| General disorders and administration site conditions  |                                                                  |                                                          |                                                             |
| Asthenia                                              |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 9 / 43 (20.93%)                                                  | 6 / 43 (13.95%)                                          | 5 / 57 (8.77%)                                              |
| occurrences (all)                                     | 10                                                               | 8                                                        | 5                                                           |
| Pain                                                  |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 0 / 43 (0.00%)                                                   | 1 / 43 (2.33%)                                           | 1 / 57 (1.75%)                                              |
| occurrences (all)                                     | 0                                                                | 1                                                        | 1                                                           |
| Oedema peripheral                                     |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 2 / 43 (4.65%)                                                   | 1 / 43 (2.33%)                                           | 1 / 57 (1.75%)                                              |
| occurrences (all)                                     | 2                                                                | 1                                                        | 3                                                           |
| Fatigue                                               |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 8 / 43 (18.60%)                                                  | 10 / 43 (23.26%)                                         | 11 / 57 (19.30%)                                            |
| occurrences (all)                                     | 12                                                               | 12                                                       | 11                                                          |
| Pyrexia                                               |                                                                  |                                                          |                                                             |
| subjects affected / exposed                           | 6 / 43 (13.95%)                                                  | 3 / 43 (6.98%)                                           | 7 / 57 (12.28%)                                             |
| occurrences (all)                                     | 6                                                                | 5                                                        | 8                                                           |
| Mucosal inflammation                                  |                                                                  |                                                          |                                                             |

|                                                                                                              |                      |                      |                      |
|--------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                             | 6 / 43 (13.95%)<br>7 | 3 / 43 (6.98%)<br>3  | 6 / 57 (10.53%)<br>7 |
| Oedema<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 43 (0.00%)<br>0  | 1 / 43 (2.33%)<br>1  | 2 / 57 (3.51%)<br>2  |
| Illness<br>subjects affected / exposed<br>occurrences (all)                                                  | 3 / 43 (6.98%)<br>9  | 0 / 43 (0.00%)<br>0  | 0 / 57 (0.00%)<br>0  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 43 (0.00%)<br>0  | 1 / 43 (2.33%)<br>1  | 0 / 57 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Breast pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 43 (0.00%)<br>0  | 2 / 43 (4.65%)<br>2  | 2 / 57 (3.51%)<br>2  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 4 / 43 (9.30%)<br>4  | 5 / 43 (11.63%)<br>5 | 3 / 57 (5.26%)<br>4  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                 | 2 / 43 (4.65%)<br>3  | 3 / 43 (6.98%)<br>3  | 3 / 57 (5.26%)<br>3  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                                              | 4 / 43 (9.30%)<br>4  | 1 / 43 (2.33%)<br>1  | 1 / 57 (1.75%)<br>1  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                                                | 3 / 43 (6.98%)<br>3  | 1 / 43 (2.33%)<br>1  | 1 / 57 (1.75%)<br>1  |
| Pneumonitis<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 43 (0.00%)<br>0  | 0 / 43 (0.00%)<br>0  | 1 / 57 (1.75%)<br>2  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                        | 4 / 43 (9.30%)<br>4  | 6 / 43 (13.95%)<br>6 | 4 / 57 (7.02%)<br>4  |
| Anxiety                                                                                                      |                      |                      |                      |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 | 0 / 43 (0.00%)<br>0 | 1 / 57 (1.75%)<br>1 |
| Investigations                                   |                     |                     |                     |
| Blood lactate dehydrogenase increased            |                     |                     |                     |
| subjects affected / exposed                      | 1 / 43 (2.33%)      | 6 / 43 (13.95%)     | 0 / 57 (0.00%)      |
| occurrences (all)                                | 1                   | 14                  | 0                   |
| Blood alkaline phosphatase increased             |                     |                     |                     |
| subjects affected / exposed                      | 5 / 43 (11.63%)     | 6 / 43 (13.95%)     | 1 / 57 (1.75%)      |
| occurrences (all)                                | 7                   | 9                   | 1                   |
| Gamma-glutamyltransferase increased              |                     |                     |                     |
| subjects affected / exposed                      | 4 / 43 (9.30%)      | 2 / 43 (4.65%)      | 1 / 57 (1.75%)      |
| occurrences (all)                                | 5                   | 4                   | 1                   |
| Weight decreased                                 |                     |                     |                     |
| subjects affected / exposed                      | 4 / 43 (9.30%)      | 0 / 43 (0.00%)      | 1 / 57 (1.75%)      |
| occurrences (all)                                | 4                   | 0                   | 1                   |
| Neutrophil count decreased                       |                     |                     |                     |
| subjects affected / exposed                      | 5 / 43 (11.63%)     | 9 / 43 (20.93%)     | 6 / 57 (10.53%)     |
| occurrences (all)                                | 12                  | 14                  | 16                  |
| Lymphocyte count decreased                       |                     |                     |                     |
| subjects affected / exposed                      | 3 / 43 (6.98%)      | 1 / 43 (2.33%)      | 1 / 57 (1.75%)      |
| occurrences (all)                                | 16                  | 9                   | 1                   |
| Lipase increased                                 |                     |                     |                     |
| subjects affected / exposed                      | 1 / 43 (2.33%)      | 1 / 43 (2.33%)      | 1 / 57 (1.75%)      |
| occurrences (all)                                | 4                   | 1                   | 1                   |
| Aspartate aminotransferase increased             |                     |                     |                     |
| subjects affected / exposed                      | 7 / 43 (16.28%)     | 10 / 43 (23.26%)    | 10 / 57 (17.54%)    |
| occurrences (all)                                | 9                   | 14                  | 18                  |
| Blood creatinine increased                       |                     |                     |                     |
| subjects affected / exposed                      | 5 / 43 (11.63%)     | 2 / 43 (4.65%)      | 1 / 57 (1.75%)      |
| occurrences (all)                                | 7                   | 2                   | 2                   |
| White blood cell count decreased                 |                     |                     |                     |
| subjects affected / exposed                      | 5 / 43 (11.63%)     | 6 / 43 (13.95%)     | 2 / 57 (3.51%)      |
| occurrences (all)                                | 13                  | 14                  | 10                  |
| Alanine aminotransferase increased               |                     |                     |                     |

|                                                                                                    |                        |                        |                        |
|----------------------------------------------------------------------------------------------------|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                                   | 11 / 43 (25.58%)<br>15 | 11 / 43 (25.58%)<br>12 | 11 / 57 (19.30%)<br>18 |
| Blood albumin decreased<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 43 (2.33%)<br>2    | 2 / 43 (4.65%)<br>2    | 0 / 57 (0.00%)<br>0    |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 43 (0.00%)<br>0    | 0 / 43 (0.00%)<br>0    | 2 / 57 (3.51%)<br>2    |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 43 (2.33%)<br>1    | 1 / 43 (2.33%)<br>4    | 2 / 57 (3.51%)<br>3    |
| Blood thyroid stimulating hormone<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0    | 2 / 43 (4.65%)<br>4    | 1 / 57 (1.75%)<br>1    |
| Glycosylated haemoglobin increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 43 (2.33%)<br>1    | 2 / 43 (4.65%)<br>2    | 0 / 57 (0.00%)<br>0    |
| Blood glucose increased<br>subjects affected / exposed<br>occurrences (all)                        | 2 / 43 (4.65%)<br>2    | 2 / 43 (4.65%)<br>4    | 0 / 57 (0.00%)<br>0    |
| Injury, poisoning and procedural<br>complications                                                  |                        |                        |                        |
| Accidental overdose<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 43 (2.33%)<br>1    | 4 / 43 (9.30%)<br>5    | 1 / 57 (1.75%)<br>1    |
| Infusion related reaction<br>subjects affected / exposed<br>occurrences (all)                      | 3 / 43 (6.98%)<br>5    | 1 / 43 (2.33%)<br>2    | 5 / 57 (8.77%)<br>7    |
| Nervous system disorders                                                                           |                        |                        |                        |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                                      | 4 / 43 (9.30%)<br>4    | 4 / 43 (9.30%)<br>4    | 4 / 57 (7.02%)<br>4    |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                       | 2 / 43 (4.65%)<br>2    | 6 / 43 (13.95%)<br>6   | 12 / 57 (21.05%)<br>14 |
| Dysgeusia                                                                                          |                        |                        |                        |

|                                      |                  |                 |                  |
|--------------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed          | 0 / 43 (0.00%)   | 1 / 43 (2.33%)  | 2 / 57 (3.51%)   |
| occurrences (all)                    | 0                | 1               | 2                |
| Neuropathy peripheral                |                  |                 |                  |
| subjects affected / exposed          | 15 / 43 (34.88%) | 8 / 43 (18.60%) | 8 / 57 (14.04%)  |
| occurrences (all)                    | 19               | 9               | 9                |
| Peripheral sensory neuropathy        |                  |                 |                  |
| subjects affected / exposed          | 4 / 43 (9.30%)   | 6 / 43 (13.95%) | 9 / 57 (15.79%)  |
| occurrences (all)                    | 4                | 7               | 10               |
| Polyneuropathy                       |                  |                 |                  |
| subjects affected / exposed          | 2 / 43 (4.65%)   | 3 / 43 (6.98%)  | 0 / 57 (0.00%)   |
| occurrences (all)                    | 2                | 3               | 0                |
| Paraesthesia                         |                  |                 |                  |
| subjects affected / exposed          | 5 / 43 (11.63%)  | 3 / 43 (6.98%)  | 1 / 57 (1.75%)   |
| occurrences (all)                    | 6                | 3               | 1                |
| Syncope                              |                  |                 |                  |
| subjects affected / exposed          | 0 / 43 (0.00%)   | 0 / 43 (0.00%)  | 1 / 57 (1.75%)   |
| occurrences (all)                    | 0                | 0               | 1                |
| Neurotoxicity                        |                  |                 |                  |
| subjects affected / exposed          | 1 / 43 (2.33%)   | 1 / 43 (2.33%)  | 2 / 57 (3.51%)   |
| occurrences (all)                    | 1                | 1               | 2                |
| Blood and lymphatic system disorders |                  |                 |                  |
| Leukopenia                           |                  |                 |                  |
| subjects affected / exposed          | 4 / 43 (9.30%)   | 2 / 43 (4.65%)  | 4 / 57 (7.02%)   |
| occurrences (all)                    | 5                | 2               | 7                |
| Anaemia                              |                  |                 |                  |
| subjects affected / exposed          | 15 / 43 (34.88%) | 7 / 43 (16.28%) | 12 / 57 (21.05%) |
| occurrences (all)                    | 22               | 18              | 17               |
| Neutropenia                          |                  |                 |                  |
| subjects affected / exposed          | 15 / 43 (34.88%) | 5 / 43 (11.63%) | 9 / 57 (15.79%)  |
| occurrences (all)                    | 21               | 21              | 19               |
| Lymphopenia                          |                  |                 |                  |
| subjects affected / exposed          | 2 / 43 (4.65%)   | 0 / 43 (0.00%)  | 1 / 57 (1.75%)   |
| occurrences (all)                    | 3                | 0               | 1                |
| Gastrointestinal disorders           |                  |                 |                  |
| Abdominal distension                 |                  |                 |                  |

|                                  |                  |                  |                  |
|----------------------------------|------------------|------------------|------------------|
| subjects affected / exposed      | 0 / 43 (0.00%)   | 1 / 43 (2.33%)   | 3 / 57 (5.26%)   |
| occurrences (all)                | 0                | 1                | 3                |
| Stomatitis                       |                  |                  |                  |
| subjects affected / exposed      | 3 / 43 (6.98%)   | 6 / 43 (13.95%)  | 3 / 57 (5.26%)   |
| occurrences (all)                | 3                | 7                | 4                |
| Dyspepsia                        |                  |                  |                  |
| subjects affected / exposed      | 3 / 43 (6.98%)   | 3 / 43 (6.98%)   | 0 / 57 (0.00%)   |
| occurrences (all)                | 4                | 3                | 0                |
| Vomiting                         |                  |                  |                  |
| subjects affected / exposed      | 7 / 43 (16.28%)  | 10 / 43 (23.26%) | 8 / 57 (14.04%)  |
| occurrences (all)                | 16               | 14               | 9                |
| Abdominal pain upper             |                  |                  |                  |
| subjects affected / exposed      | 5 / 43 (11.63%)  | 0 / 43 (0.00%)   | 3 / 57 (5.26%)   |
| occurrences (all)                | 7                | 0                | 3                |
| Abdominal pain                   |                  |                  |                  |
| subjects affected / exposed      | 2 / 43 (4.65%)   | 4 / 43 (9.30%)   | 2 / 57 (3.51%)   |
| occurrences (all)                | 2                | 4                | 2                |
| Diarrhoea                        |                  |                  |                  |
| subjects affected / exposed      | 32 / 43 (74.42%) | 30 / 43 (69.77%) | 16 / 57 (28.07%) |
| occurrences (all)                | 66               | 71               | 28               |
| Nausea                           |                  |                  |                  |
| subjects affected / exposed      | 17 / 43 (39.53%) | 14 / 43 (32.56%) | 13 / 57 (22.81%) |
| occurrences (all)                | 21               | 16               | 16               |
| Constipation                     |                  |                  |                  |
| subjects affected / exposed      | 7 / 43 (16.28%)  | 12 / 43 (27.91%) | 24 / 57 (42.11%) |
| occurrences (all)                | 7                | 16               | 33               |
| Gastritis                        |                  |                  |                  |
| subjects affected / exposed      | 1 / 43 (2.33%)   | 1 / 43 (2.33%)   | 1 / 57 (1.75%)   |
| occurrences (all)                | 1                | 1                | 1                |
| Dry mouth                        |                  |                  |                  |
| subjects affected / exposed      | 1 / 43 (2.33%)   | 1 / 43 (2.33%)   | 0 / 57 (0.00%)   |
| occurrences (all)                | 1                | 1                | 0                |
| Abdominal discomfort             |                  |                  |                  |
| subjects affected / exposed      | 3 / 43 (6.98%)   | 0 / 43 (0.00%)   | 1 / 57 (1.75%)   |
| occurrences (all)                | 3                | 0                | 1                |
| Gastrooesophageal reflux disease |                  |                  |                  |

|                                                                                                                  |                        |                        |                        |
|------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                 | 3 / 43 (6.98%)<br>5    | 2 / 43 (4.65%)<br>2    | 0 / 57 (0.00%)<br>0    |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)               | 3 / 43 (6.98%)<br>4    | 0 / 43 (0.00%)<br>0    | 0 / 57 (0.00%)<br>0    |
| Skin and subcutaneous tissue disorders<br>Erythema<br>subjects affected / exposed<br>occurrences (all)           | 2 / 43 (4.65%)<br>2    | 2 / 43 (4.65%)<br>2    | 3 / 57 (5.26%)<br>3    |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                     | 3 / 43 (6.98%)<br>4    | 0 / 43 (0.00%)<br>0    | 8 / 57 (14.04%)<br>8   |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)                                                    | 4 / 43 (9.30%)<br>4    | 0 / 43 (0.00%)<br>0    | 3 / 57 (5.26%)<br>3    |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                                     | 10 / 43 (23.26%)<br>10 | 13 / 43 (30.23%)<br>13 | 25 / 57 (43.86%)<br>26 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 43 (2.33%)<br>1    | 4 / 43 (9.30%)<br>5    | 0 / 57 (0.00%)<br>0    |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                                         | 10 / 43 (23.26%)<br>11 | 10 / 43 (23.26%)<br>15 | 17 / 57 (29.82%)<br>35 |
| Endocrine disorders<br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 43 (0.00%)<br>0    | 0 / 43 (0.00%)<br>0    | 4 / 57 (7.02%)<br>5    |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                                               | 2 / 43 (4.65%)<br>2    | 2 / 43 (4.65%)<br>2    | 6 / 57 (10.53%)<br>7   |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all) | 3 / 43 (6.98%)<br>3    | 4 / 43 (9.30%)<br>5    | 5 / 57 (8.77%)<br>6    |

|                                                                                                            |                      |                       |                      |
|------------------------------------------------------------------------------------------------------------|----------------------|-----------------------|----------------------|
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                                             | 4 / 43 (9.30%)<br>4  | 4 / 43 (9.30%)<br>5   | 4 / 57 (7.02%)<br>9  |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)                                              | 2 / 43 (4.65%)<br>2  | 2 / 43 (4.65%)<br>3   | 1 / 57 (1.75%)<br>2  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 43 (2.33%)<br>1  | 1 / 43 (2.33%)<br>1   | 0 / 57 (0.00%)<br>0  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                                                | 5 / 43 (11.63%)<br>5 | 3 / 43 (6.98%)<br>3   | 5 / 57 (8.77%)<br>5  |
| Infections and infestations<br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 43 (6.98%)<br>3  | 4 / 43 (9.30%)<br>4   | 2 / 57 (3.51%)<br>3  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)                                               | 2 / 43 (4.65%)<br>2  | 2 / 43 (4.65%)<br>2   | 3 / 57 (5.26%)<br>3  |
| Metabolism and nutrition disorders<br>Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)    | 1 / 43 (2.33%)<br>4  | 3 / 43 (6.98%)<br>3   | 1 / 57 (1.75%)<br>1  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                                     | 6 / 43 (13.95%)<br>7 | 6 / 43 (13.95%)<br>6  | 7 / 57 (12.28%)<br>9 |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 43 (2.33%)<br>1  | 1 / 43 (2.33%)<br>1   | 3 / 57 (5.26%)<br>4  |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 43 (0.00%)<br>0  | 5 / 43 (11.63%)<br>11 | 1 / 57 (1.75%)<br>1  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                                           | 4 / 43 (9.30%)<br>6  | 0 / 43 (0.00%)<br>0   | 1 / 57 (1.75%)<br>1  |
| Hyperglycaemia                                                                                             |                      |                       |                      |

|                             |                  |                |                |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 10 / 43 (23.26%) | 4 / 43 (9.30%) | 3 / 57 (5.26%) |
| occurrences (all)           | 12               | 9              | 4              |
| Hyponatraemia               |                  |                |                |
| subjects affected / exposed | 2 / 43 (4.65%)   | 1 / 43 (2.33%) | 0 / 57 (0.00%) |
| occurrences (all)           | 2                | 1              | 0              |
| Hypomagnesaemia             |                  |                |                |
| subjects affected / exposed | 3 / 43 (6.98%)   | 0 / 43 (0.00%) | 1 / 57 (1.75%) |
| occurrences (all)           | 3                | 0              | 1              |
| Hypernatraemia              |                  |                |                |
| subjects affected / exposed | 1 / 43 (2.33%)   | 2 / 43 (4.65%) | 0 / 57 (0.00%) |
| occurrences (all)           | 2                | 2              | 0              |
| Dehydration                 |                  |                |                |
| subjects affected / exposed | 0 / 43 (0.00%)   | 2 / 43 (4.65%) | 0 / 57 (0.00%) |
| occurrences (all)           | 0                | 2              | 0              |

| <b>Non-serious adverse events</b>                     | Cohort 2 Arm A:<br>Ipatasertib +<br>Atezolizumab +<br>Paclitaxel | Cohort 1 Arm C:<br>Placebo + Placebo +<br>Paclitaxel |  |
|-------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------|--|
| Total subjects affected by non-serious adverse events |                                                                  |                                                      |  |
| subjects affected / exposed                           | 56 / 58 (96.55%)                                                 | 40 / 41 (97.56%)                                     |  |
| Vascular disorders                                    |                                                                  |                                                      |  |
| Lymphoedema                                           |                                                                  |                                                      |  |
| subjects affected / exposed                           | 1 / 58 (1.72%)                                                   | 0 / 41 (0.00%)                                       |  |
| occurrences (all)                                     | 1                                                                | 0                                                    |  |
| Hypertension                                          |                                                                  |                                                      |  |
| subjects affected / exposed                           | 4 / 58 (6.90%)                                                   | 2 / 41 (4.88%)                                       |  |
| occurrences (all)                                     | 5                                                                | 2                                                    |  |
| General disorders and administration site conditions  |                                                                  |                                                      |  |
| Asthenia                                              |                                                                  |                                                      |  |
| subjects affected / exposed                           | 13 / 58 (22.41%)                                                 | 7 / 41 (17.07%)                                      |  |
| occurrences (all)                                     | 24                                                               | 9                                                    |  |
| Pain                                                  |                                                                  |                                                      |  |
| subjects affected / exposed                           | 3 / 58 (5.17%)                                                   | 3 / 41 (7.32%)                                       |  |
| occurrences (all)                                     | 3                                                                | 4                                                    |  |
| Oedema peripheral                                     |                                                                  |                                                      |  |
| subjects affected / exposed                           | 4 / 58 (6.90%)                                                   | 4 / 41 (9.76%)                                       |  |
| occurrences (all)                                     | 5                                                                | 6                                                    |  |

|                                                 |                  |                 |  |
|-------------------------------------------------|------------------|-----------------|--|
| Fatigue                                         |                  |                 |  |
| subjects affected / exposed                     | 14 / 58 (24.14%) | 5 / 41 (12.20%) |  |
| occurrences (all)                               | 15               | 8               |  |
| Pyrexia                                         |                  |                 |  |
| subjects affected / exposed                     | 7 / 58 (12.07%)  | 1 / 41 (2.44%)  |  |
| occurrences (all)                               | 10               | 2               |  |
| Mucosal inflammation                            |                  |                 |  |
| subjects affected / exposed                     | 4 / 58 (6.90%)   | 0 / 41 (0.00%)  |  |
| occurrences (all)                               | 5                | 0               |  |
| Oedema                                          |                  |                 |  |
| subjects affected / exposed                     | 4 / 58 (6.90%)   | 0 / 41 (0.00%)  |  |
| occurrences (all)                               | 4                | 0               |  |
| Illness                                         |                  |                 |  |
| subjects affected / exposed                     | 0 / 58 (0.00%)   | 0 / 41 (0.00%)  |  |
| occurrences (all)                               | 0                | 0               |  |
| Malaise                                         |                  |                 |  |
| subjects affected / exposed                     | 3 / 58 (5.17%)   | 1 / 41 (2.44%)  |  |
| occurrences (all)                               | 3                | 1               |  |
| Reproductive system and breast disorders        |                  |                 |  |
| Breast pain                                     |                  |                 |  |
| subjects affected / exposed                     | 3 / 58 (5.17%)   | 4 / 41 (9.76%)  |  |
| occurrences (all)                               | 3                | 4               |  |
| Respiratory, thoracic and mediastinal disorders |                  |                 |  |
| Cough                                           |                  |                 |  |
| subjects affected / exposed                     | 4 / 58 (6.90%)   | 0 / 41 (0.00%)  |  |
| occurrences (all)                               | 5                | 0               |  |
| Dyspnoea                                        |                  |                 |  |
| subjects affected / exposed                     | 5 / 58 (8.62%)   | 4 / 41 (9.76%)  |  |
| occurrences (all)                               | 5                | 4               |  |
| Rhinorrhoea                                     |                  |                 |  |
| subjects affected / exposed                     | 1 / 58 (1.72%)   | 0 / 41 (0.00%)  |  |
| occurrences (all)                               | 1                | 0               |  |
| Epistaxis                                       |                  |                 |  |
| subjects affected / exposed                     | 1 / 58 (1.72%)   | 1 / 41 (2.44%)  |  |
| occurrences (all)                               | 1                | 1               |  |
| Pneumonitis                                     |                  |                 |  |

|                                                  |                     |                     |  |
|--------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 3 / 58 (5.17%)<br>3 | 0 / 41 (0.00%)<br>0 |  |
| Psychiatric disorders                            |                     |                     |  |
| Insomnia                                         |                     |                     |  |
| subjects affected / exposed                      | 6 / 58 (10.34%)     | 3 / 41 (7.32%)      |  |
| occurrences (all)                                | 6                   | 3                   |  |
| Anxiety                                          |                     |                     |  |
| subjects affected / exposed                      | 3 / 58 (5.17%)      | 0 / 41 (0.00%)      |  |
| occurrences (all)                                | 3                   | 0                   |  |
| Investigations                                   |                     |                     |  |
| Blood lactate dehydrogenase increased            |                     |                     |  |
| subjects affected / exposed                      | 3 / 58 (5.17%)      | 1 / 41 (2.44%)      |  |
| occurrences (all)                                | 7                   | 1                   |  |
| Blood alkaline phosphatase increased             |                     |                     |  |
| subjects affected / exposed                      | 6 / 58 (10.34%)     | 1 / 41 (2.44%)      |  |
| occurrences (all)                                | 9                   | 1                   |  |
| Gamma-glutamyltransferase increased              |                     |                     |  |
| subjects affected / exposed                      | 6 / 58 (10.34%)     | 0 / 41 (0.00%)      |  |
| occurrences (all)                                | 7                   | 0                   |  |
| Weight decreased                                 |                     |                     |  |
| subjects affected / exposed                      | 3 / 58 (5.17%)      | 1 / 41 (2.44%)      |  |
| occurrences (all)                                | 3                   | 2                   |  |
| Neutrophil count decreased                       |                     |                     |  |
| subjects affected / exposed                      | 9 / 58 (15.52%)     | 5 / 41 (12.20%)     |  |
| occurrences (all)                                | 20                  | 7                   |  |
| Lymphocyte count decreased                       |                     |                     |  |
| subjects affected / exposed                      | 3 / 58 (5.17%)      | 0 / 41 (0.00%)      |  |
| occurrences (all)                                | 10                  | 0                   |  |
| Lipase increased                                 |                     |                     |  |
| subjects affected / exposed                      | 5 / 58 (8.62%)      | 0 / 41 (0.00%)      |  |
| occurrences (all)                                | 5                   | 0                   |  |
| Aspartate aminotransferase increased             |                     |                     |  |
| subjects affected / exposed                      | 11 / 58 (18.97%)    | 10 / 41 (24.39%)    |  |
| occurrences (all)                                | 16                  | 18                  |  |
| Blood creatinine increased                       |                     |                     |  |

|                                                |                  |                  |  |
|------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                    | 5 / 58 (8.62%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                              | 8                | 0                |  |
| White blood cell count decreased               |                  |                  |  |
| subjects affected / exposed                    | 4 / 58 (6.90%)   | 1 / 41 (2.44%)   |  |
| occurrences (all)                              | 11               | 2                |  |
| Alanine aminotransferase increased             |                  |                  |  |
| subjects affected / exposed                    | 12 / 58 (20.69%) | 12 / 41 (29.27%) |  |
| occurrences (all)                              | 19               | 15               |  |
| Blood albumin decreased                        |                  |                  |  |
| subjects affected / exposed                    | 3 / 58 (5.17%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                              | 6                | 0                |  |
| Amylase increased                              |                  |                  |  |
| subjects affected / exposed                    | 4 / 58 (6.90%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                              | 4                | 0                |  |
| Blood cholesterol increased                    |                  |                  |  |
| subjects affected / exposed                    | 4 / 58 (6.90%)   | 2 / 41 (4.88%)   |  |
| occurrences (all)                              | 9                | 2                |  |
| Blood thyroid stimulating hormone increased    |                  |                  |  |
| subjects affected / exposed                    | 3 / 58 (5.17%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                              | 3                | 0                |  |
| Glycosylated haemoglobin increased             |                  |                  |  |
| subjects affected / exposed                    | 3 / 58 (5.17%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                              | 3                | 0                |  |
| Blood glucose increased                        |                  |                  |  |
| subjects affected / exposed                    | 3 / 58 (5.17%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                              | 4                | 0                |  |
| Injury, poisoning and procedural complications |                  |                  |  |
| Accidental overdose                            |                  |                  |  |
| subjects affected / exposed                    | 3 / 58 (5.17%)   | 1 / 41 (2.44%)   |  |
| occurrences (all)                              | 8                | 1                |  |
| Infusion related reaction                      |                  |                  |  |
| subjects affected / exposed                    | 8 / 58 (13.79%)  | 2 / 41 (4.88%)   |  |
| occurrences (all)                              | 11               | 2                |  |
| Nervous system disorders                       |                  |                  |  |

|                                      |                  |                  |  |
|--------------------------------------|------------------|------------------|--|
| Dizziness                            |                  |                  |  |
| subjects affected / exposed          | 5 / 58 (8.62%)   | 2 / 41 (4.88%)   |  |
| occurrences (all)                    | 5                | 11               |  |
| Headache                             |                  |                  |  |
| subjects affected / exposed          | 11 / 58 (18.97%) | 3 / 41 (7.32%)   |  |
| occurrences (all)                    | 15               | 3                |  |
| Dysgeusia                            |                  |                  |  |
| subjects affected / exposed          | 7 / 58 (12.07%)  | 3 / 41 (7.32%)   |  |
| occurrences (all)                    | 8                | 3                |  |
| Neuropathy peripheral                |                  |                  |  |
| subjects affected / exposed          | 8 / 58 (13.79%)  | 10 / 41 (24.39%) |  |
| occurrences (all)                    | 8                | 11               |  |
| Peripheral sensory neuropathy        |                  |                  |  |
| subjects affected / exposed          | 11 / 58 (18.97%) | 5 / 41 (12.20%)  |  |
| occurrences (all)                    | 11               | 6                |  |
| Polyneuropathy                       |                  |                  |  |
| subjects affected / exposed          | 0 / 58 (0.00%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Paraesthesia                         |                  |                  |  |
| subjects affected / exposed          | 4 / 58 (6.90%)   | 3 / 41 (7.32%)   |  |
| occurrences (all)                    | 5                | 3                |  |
| Syncope                              |                  |                  |  |
| subjects affected / exposed          | 3 / 58 (5.17%)   | 1 / 41 (2.44%)   |  |
| occurrences (all)                    | 3                | 1                |  |
| Neurotoxicity                        |                  |                  |  |
| subjects affected / exposed          | 3 / 58 (5.17%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)                    | 4                | 0                |  |
| Blood and lymphatic system disorders |                  |                  |  |
| Leukopenia                           |                  |                  |  |
| subjects affected / exposed          | 8 / 58 (13.79%)  | 2 / 41 (4.88%)   |  |
| occurrences (all)                    | 13               | 6                |  |
| Anaemia                              |                  |                  |  |
| subjects affected / exposed          | 22 / 58 (37.93%) | 6 / 41 (14.63%)  |  |
| occurrences (all)                    | 36               | 10               |  |
| Neutropenia                          |                  |                  |  |

|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 11 / 58 (18.97%) | 8 / 41 (19.51%)  |  |
| occurrences (all)           | 36               | 26               |  |
| Lymphopenia                 |                  |                  |  |
| subjects affected / exposed | 3 / 58 (5.17%)   | 0 / 41 (0.00%)   |  |
| occurrences (all)           | 6                | 0                |  |
| Gastrointestinal disorders  |                  |                  |  |
| Abdominal distension        |                  |                  |  |
| subjects affected / exposed | 3 / 58 (5.17%)   | 1 / 41 (2.44%)   |  |
| occurrences (all)           | 3                | 1                |  |
| Stomatitis                  |                  |                  |  |
| subjects affected / exposed | 7 / 58 (12.07%)  | 2 / 41 (4.88%)   |  |
| occurrences (all)           | 8                | 3                |  |
| Dyspepsia                   |                  |                  |  |
| subjects affected / exposed | 6 / 58 (10.34%)  | 2 / 41 (4.88%)   |  |
| occurrences (all)           | 8                | 2                |  |
| Vomiting                    |                  |                  |  |
| subjects affected / exposed | 8 / 58 (13.79%)  | 0 / 41 (0.00%)   |  |
| occurrences (all)           | 10               | 0                |  |
| Abdominal pain upper        |                  |                  |  |
| subjects affected / exposed | 5 / 58 (8.62%)   | 2 / 41 (4.88%)   |  |
| occurrences (all)           | 7                | 2                |  |
| Abdominal pain              |                  |                  |  |
| subjects affected / exposed | 4 / 58 (6.90%)   | 4 / 41 (9.76%)   |  |
| occurrences (all)           | 5                | 4                |  |
| Diarrhoea                   |                  |                  |  |
| subjects affected / exposed | 37 / 58 (63.79%) | 15 / 41 (36.59%) |  |
| occurrences (all)           | 81               | 22               |  |
| Nausea                      |                  |                  |  |
| subjects affected / exposed | 22 / 58 (37.93%) | 9 / 41 (21.95%)  |  |
| occurrences (all)           | 36               | 10               |  |
| Constipation                |                  |                  |  |
| subjects affected / exposed | 16 / 58 (27.59%) | 26 / 41 (63.41%) |  |
| occurrences (all)           | 22               | 29               |  |
| Gastritis                   |                  |                  |  |
| subjects affected / exposed | 1 / 58 (1.72%)   | 3 / 41 (7.32%)   |  |
| occurrences (all)           | 1                | 3                |  |

|                                                                                                        |                        |                        |  |
|--------------------------------------------------------------------------------------------------------|------------------------|------------------------|--|
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)                                          | 3 / 58 (5.17%)<br>3    | 0 / 41 (0.00%)<br>0    |  |
| Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 58 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0    |  |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 58 (3.45%)<br>2    | 0 / 41 (0.00%)<br>0    |  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 58 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0    |  |
| Skin and subcutaneous tissue disorders<br>Erythema<br>subjects affected / exposed<br>occurrences (all) | 0 / 58 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0    |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                           | 8 / 58 (13.79%)<br>9   | 5 / 41 (12.20%)<br>6   |  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 58 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0    |  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                           | 18 / 58 (31.03%)<br>18 | 19 / 41 (46.34%)<br>19 |  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                | 4 / 58 (6.90%)<br>4    | 0 / 41 (0.00%)<br>0    |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                               | 19 / 58 (32.76%)<br>27 | 7 / 41 (17.07%)<br>11  |  |
| Endocrine disorders<br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)             | 1 / 58 (1.72%)<br>1    | 0 / 41 (0.00%)<br>0    |  |
| Hypothyroidism                                                                                         |                        |                        |  |

|                                                  |                      |                     |  |
|--------------------------------------------------|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 6 / 58 (10.34%)<br>7 | 0 / 41 (0.00%)<br>0 |  |
| Musculoskeletal and connective tissue disorders  |                      |                     |  |
| Back pain                                        |                      |                     |  |
| subjects affected / exposed                      | 5 / 58 (8.62%)       | 2 / 41 (4.88%)      |  |
| occurrences (all)                                | 7                    | 2                   |  |
| Arthralgia                                       |                      |                     |  |
| subjects affected / exposed                      | 7 / 58 (12.07%)      | 3 / 41 (7.32%)      |  |
| occurrences (all)                                | 8                    | 3                   |  |
| Bone pain                                        |                      |                     |  |
| subjects affected / exposed                      | 5 / 58 (8.62%)       | 2 / 41 (4.88%)      |  |
| occurrences (all)                                | 5                    | 2                   |  |
| Musculoskeletal pain                             |                      |                     |  |
| subjects affected / exposed                      | 0 / 58 (0.00%)       | 3 / 41 (7.32%)      |  |
| occurrences (all)                                | 0                    | 3                   |  |
| Myalgia                                          |                      |                     |  |
| subjects affected / exposed                      | 9 / 58 (15.52%)      | 8 / 41 (19.51%)     |  |
| occurrences (all)                                | 26                   | 9                   |  |
| Infections and infestations                      |                      |                     |  |
| Urinary tract infection                          |                      |                     |  |
| subjects affected / exposed                      | 3 / 58 (5.17%)       | 2 / 41 (4.88%)      |  |
| occurrences (all)                                | 3                    | 8                   |  |
| COVID-19                                         |                      |                     |  |
| subjects affected / exposed                      | 1 / 58 (1.72%)       | 0 / 41 (0.00%)      |  |
| occurrences (all)                                | 1                    | 0                   |  |
| Metabolism and nutrition disorders               |                      |                     |  |
| Hypocalcaemia                                    |                      |                     |  |
| subjects affected / exposed                      | 1 / 58 (1.72%)       | 0 / 41 (0.00%)      |  |
| occurrences (all)                                | 1                    | 0                   |  |
| Decreased appetite                               |                      |                     |  |
| subjects affected / exposed                      | 16 / 58 (27.59%)     | 6 / 41 (14.63%)     |  |
| occurrences (all)                                | 20                   | 7                   |  |
| Hyperkalaemia                                    |                      |                     |  |
| subjects affected / exposed                      | 2 / 58 (3.45%)       | 1 / 41 (2.44%)      |  |
| occurrences (all)                                | 4                    | 1                   |  |
| Hypertriglyceridaemia                            |                      |                     |  |

|                             |                  |                |  |
|-----------------------------|------------------|----------------|--|
| subjects affected / exposed | 5 / 58 (8.62%)   | 0 / 41 (0.00%) |  |
| occurrences (all)           | 5                | 0              |  |
| Hypokalaemia                |                  |                |  |
| subjects affected / exposed | 6 / 58 (10.34%)  | 1 / 41 (2.44%) |  |
| occurrences (all)           | 8                | 1              |  |
| Hyperglycaemia              |                  |                |  |
| subjects affected / exposed | 12 / 58 (20.69%) | 2 / 41 (4.88%) |  |
| occurrences (all)           | 18               | 2              |  |
| Hyponatraemia               |                  |                |  |
| subjects affected / exposed | 4 / 58 (6.90%)   | 2 / 41 (4.88%) |  |
| occurrences (all)           | 5                | 2              |  |
| Hypomagnesaemia             |                  |                |  |
| subjects affected / exposed | 1 / 58 (1.72%)   | 2 / 41 (4.88%) |  |
| occurrences (all)           | 1                | 2              |  |
| Hypernatraemia              |                  |                |  |
| subjects affected / exposed | 3 / 58 (5.17%)   | 0 / 41 (0.00%) |  |
| occurrences (all)           | 6                | 0              |  |
| Dehydration                 |                  |                |  |
| subjects affected / exposed | 3 / 58 (5.17%)   | 0 / 41 (0.00%) |  |
| occurrences (all)           | 3                | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 13 September 2019 | Amendment 1: 1. Disease-specific inclusion criteria was updated to include a criterion that a participant must be an appropriate candidate for paclitaxel monotherapy if tumor PD-L1 status is unknown and if tumor status is known to be PD-L1 positive, the participant should be an appropriate candidate for atezolizumab+paclitaxel.<br>2. General exclusion criteria was updated to include a criterion that a participant must not be on current treatment with medications used at doses known to cause clinically relevant prolongation of QT/corrected QT (QTc) interval.<br>3. Disease-specific exclusion criteria have been updated to include a criterion that a participant must not have known germline breast cancer gene (BRCA)1/2 deleterious mutation.<br>4. The Optional Interim Analyses section (Section 6.9.3) was removed. |
| 20 September 2019 | Amendment 2: 1. Enrolment number was updated from 1150 to 1155 participants, with a change from approximately 520 to approximately 525 participants in Cohort 1. The allocation of participants between arms in Cohort 1 was made equal, to support the independent testing of Arm A vs. Arm C, and Arm B vs. Arm C.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 18 August 2020    | Amendment 3: 1. The study rationale and benefit-risk assessment was updated to indicate that based on results from the primary analysis of the MO39196 study, the control arm for Cohort 2 of this Study CO41101 (atezolizumab plus paclitaxel plus placebo for ipatasertib) was no longer considered appropriate. As of 6 August 2020, further enrollment in Cohort 2 was suspended, and all participants in Cohort 2 were unblinded to treatment assignment.                                                                                                                                                                                                                                                                                                                                                                                     |
| 21 December 2020  | Amendment 4: 1. Section 1.2 was updated to include the outcome of the primary analysis of the CO40016 study and rationale for termination of enrollment and unblinding of Cohort 1 of Study CO41101.<br>2. Study was updated to indicate that based on results from the primary analysis of the CO40016 study in TNBC, Arm B for Cohort 1 of this Study CO41101 (ipatasertib plus paclitaxel plus placebo for atezolizumab) was no longer considered appropriate. As of 18 September 2020, further enrollment in Cohort 1 was terminated, and all participants in Cohort 1 were unblinded to treatment assignment on 21 September 2020.<br>3. All secondary efficacy objectives and pharmacokinetic and immunogenicity objectives were moved to exploratory objectives.<br>4. The total length of the study was changed to 2-3 years.              |
| 25 February 2022  | Amendment 5: 1. Benefit-risk assessment and guidance on concomitant administration of severe acute respiratory syndrome coronavirus 2 vaccines with atezolizumab was added.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported