



## Clinical trial results:

### A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Immunotherapy-Based Treatment Combinations in Patients With Metastatic Colorectal Cancer (Morpheus-CRC)

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2017-004566-99    |
| Trial protocol           | GB ES             |
| Global end of trial date | 26 September 2022 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 08 October 2023 |
| First version publication date | 08 October 2023 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | CO39612 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03555149 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                    |
|------------------------------|----------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | F. Hoffmann-La Roche AG                                                                            |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070                                                 |
| Public contact               | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact           | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                   |
|------------------------------------------------------|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 26 September 2022 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 26 September 2022 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 26 September 2022 |
| Was the trial ended prematurely?                     | Yes               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy, safety, and pharmacokinetics of multiple immunotherapy-based treatment combinations in patients with metastatic colorectal cancer (mCRC).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 27 September 2018 |
| Long term follow-up planned                               | Yes               |
| Long term follow-up rationale                             | Efficacy, Safety  |
| Long term follow-up duration                              | 4 Years           |
| Independent data monitoring committee (IDMC) involvement? | No                |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Switzerland: 2         |
| Country: Number of subjects enrolled | France: 16             |
| Country: Number of subjects enrolled | Korea, Republic of: 27 |
| Country: Number of subjects enrolled | United States: 45      |
| Country: Number of subjects enrolled | Australia: 6           |
| Worldwide total number of subjects   | 96                     |
| EEA total number of subjects         | 16                     |

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) | 72 |
| From 65 to 84 years  | 24 |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 15 centers in 5 countries: United States, France, Republic of Korea, Australia, and Switzerland.

### Pre-assignment

Screening details:

A total of 96 participants were enrolled.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Regorafenib (Control) |

Arm description:

Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Active comparator  |
| Investigational medicinal product name | Regorafenib        |
| Investigational medicinal product code | RO7069680          |
| Other name                             | Stivarga           |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

160 mg once daily on Days 1-21 of each cycle (21 day cycle)

|                  |                                          |
|------------------|------------------------------------------|
| <b>Arm title</b> | Atezolizumab + Imprime PGG + Bevacizumab |
|------------------|------------------------------------------|

Arm description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Atezolizumab                          |
| Investigational medicinal product code | RO5541267                             |
| Other name                             | Tecentriq                             |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

1200 mg IV on Day 1 of each cycle (21 day cycle)

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Investigational medicinal product name | Bevacizumab                           |
| Investigational medicinal product code |                                       |
| Other name                             | Avastin                               |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

7.5 mg/kg on Day 1 of each cycle (21 day cycle)

|                                                                                                                                                                                                                 |                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| Investigational medicinal product name                                                                                                                                                                          | Imprime PGG                                     |
| Investigational medicinal product code                                                                                                                                                                          | RO7234832                                       |
| Other name                                                                                                                                                                                                      | PGG beta glucan                                 |
| Pharmaceutical forms                                                                                                                                                                                            | Solution for infusion                           |
| Routes of administration                                                                                                                                                                                        | Intravenous use                                 |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 4 mg/kg on Days 1, 8 and 15 of each cycle (21 day cycle)                                                                                                                                                        |                                                 |
| <b>Arm title</b>                                                                                                                                                                                                | Atezolizumab + Isatuximab                       |
| Arm description:                                                                                                                                                                                                |                                                 |
| Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                                 |
| Arm type                                                                                                                                                                                                        | Experimental                                    |
| Investigational medicinal product name                                                                                                                                                                          | Isatuximab                                      |
| Investigational medicinal product code                                                                                                                                                                          | RO7268598                                       |
| Other name                                                                                                                                                                                                      | SAR650984                                       |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for infusion           |
| Routes of administration                                                                                                                                                                                        | Intravenous use                                 |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 10 mg/kg on Days 1, 8, and 15 for Cycle 1 (21 day cycle)                                                                                                                                                        |                                                 |
| 10 mg/kg on Day 1 of each cycle Cycle 2+ (21 day cycle)                                                                                                                                                         |                                                 |
| Investigational medicinal product name                                                                                                                                                                          | Atezolizumab                                    |
| Investigational medicinal product code                                                                                                                                                                          | RO5541267                                       |
| Other name                                                                                                                                                                                                      | Tecentriq                                       |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for infusion           |
| Routes of administration                                                                                                                                                                                        | Intravenous use                                 |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 1200 mg on Day 1 of each cycle (21 day cycle)                                                                                                                                                                   |                                                 |
| <b>Arm title</b>                                                                                                                                                                                                | Atezolizumab + Selicrelumab + Bevacizumab       |
| Arm description:                                                                                                                                                                                                |                                                 |
| Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                                 |
| Arm type                                                                                                                                                                                                        | Experimental                                    |
| Investigational medicinal product name                                                                                                                                                                          | Atezolizumab                                    |
| Investigational medicinal product code                                                                                                                                                                          | RO5541267                                       |
| Other name                                                                                                                                                                                                      | Tecentriq                                       |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for infusion           |
| Routes of administration                                                                                                                                                                                        | Intravenous use                                 |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 840 mg on Days 1 and 15 of each cycle (28 day cycle)                                                                                                                                                            |                                                 |
| Investigational medicinal product name                                                                                                                                                                          | Bevacizumab                                     |
| Investigational medicinal product code                                                                                                                                                                          |                                                 |
| Other name                                                                                                                                                                                                      | Avastin                                         |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for infusion           |
| Routes of administration                                                                                                                                                                                        | Intravenous use                                 |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 10 mg/kg on Days 1 and 15 of each cycle (28 day cycle)                                                                                                                                                          |                                                 |
| Investigational medicinal product name                                                                                                                                                                          | Selicrelumab                                    |
| Investigational medicinal product code                                                                                                                                                                          | RO7009789                                       |
| Other name                                                                                                                                                                                                      | CD40                                            |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for injection/infusion |
| Routes of administration                                                                                                                                                                                        | Subcutaneous use                                |

**Dosage and administration details:**

16 mg SC on Day 1 of Cycles 1-4 and every third cycle there after (i.e., Cycles 7, 10, 13, etc. ) (28 day cycle)

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Atezolizumab + Idasanutlin |
|------------------|----------------------------|

**Arm description:**

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                                        |               |
|----------------------------------------|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Idasanutlin   |
| Investigational medicinal product code | RO5503781/F33 |
| Other name                             |               |
| Pharmaceutical forms                   | Tablet        |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

150 mg once daily on Days 1-5 (28 day cycle)

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Investigational medicinal product name | Atezolizumab                          |
| Investigational medicinal product code | RO5541267                             |
| Other name                             | Tecentriq                             |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

840 mg on Days 1 and 15 of each cycle (28 day cycle)

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Atezolizumab + Regorafenib |
|------------------|----------------------------|

**Arm description:**

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Regorafenib        |
| Investigational medicinal product code | RO7069680          |
| Other name                             | Stivarga           |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

120 mg once daily on Days 1-21 of each cycle (28 day cycle)

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Investigational medicinal product name | Atezolizumab                          |
| Investigational medicinal product code | RO5541267                             |
| Other name                             | Tecentriq                             |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

840 mg on Days 1 and 15 of each cycle (28 day cycle)

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | Atezolizumab + Regorafenib + AB928 |
|------------------|------------------------------------|

**Arm description:**

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                                                                                                                                                                                                 |                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| Investigational medicinal product name                                                                                                                                                                          | Atezolizumab                                    |
| Investigational medicinal product code                                                                                                                                                                          | RO5541267                                       |
| Other name                                                                                                                                                                                                      | Tecentriq                                       |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for infusion           |
| Routes of administration                                                                                                                                                                                        | Oral use                                        |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 840 mg on Days 1 and 15 of each cycle (28 day cycle)                                                                                                                                                            |                                                 |
| Investigational medicinal product name                                                                                                                                                                          | Etrumadenant                                    |
| Investigational medicinal product code                                                                                                                                                                          | AB928                                           |
| Other name                                                                                                                                                                                                      |                                                 |
| Pharmaceutical forms                                                                                                                                                                                            | Capsule                                         |
| Routes of administration                                                                                                                                                                                        | Oral use                                        |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 150 mg once daily on Days 1-28 of each cycle (28 day cycle)                                                                                                                                                     |                                                 |
| Investigational medicinal product name                                                                                                                                                                          | Regorafenib                                     |
| Investigational medicinal product code                                                                                                                                                                          | RO7069680                                       |
| Other name                                                                                                                                                                                                      | Stivarga                                        |
| Pharmaceutical forms                                                                                                                                                                                            | Film-coated tablet                              |
| Routes of administration                                                                                                                                                                                        | Oral use                                        |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 120 mg once daily on Days 1-21 of each cycle (28 day cycle)                                                                                                                                                     |                                                 |
| <b>Arm title</b>                                                                                                                                                                                                | Atezolizumab + LOAd703                          |
| Arm description:                                                                                                                                                                                                |                                                 |
| Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                                 |
| Arm type                                                                                                                                                                                                        | Experimental                                    |
| Investigational medicinal product name                                                                                                                                                                          | LOAd703                                         |
| Investigational medicinal product code                                                                                                                                                                          |                                                 |
| Other name                                                                                                                                                                                                      | delolimogene mupadenorepvec                     |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for injection/infusion |
| Routes of administration                                                                                                                                                                                        | Intratumoral use                                |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 1 x 10 <sup>11</sup> VP or 5 x 10 <sup>11</sup> VP on Day 1 (21 day cycle)                                                                                                                                      |                                                 |
| Investigational medicinal product name                                                                                                                                                                          | Atezolizumab                                    |
| Investigational medicinal product code                                                                                                                                                                          | RO5541267                                       |
| Other name                                                                                                                                                                                                      | Tecentriq                                       |
| Pharmaceutical forms                                                                                                                                                                                            | Concentrate for solution for infusion           |
| Routes of administration                                                                                                                                                                                        | Intravenous use                                 |
| Dosage and administration details:                                                                                                                                                                              |                                                 |
| 1200 mg on Day 1 of each cycle (21 day cycle)                                                                                                                                                                   |                                                 |

| Number of subjects in period 1        | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab |
|---------------------------------------|-----------------------|------------------------------------------|---------------------------|
|                                       |                       |                                          |                           |
| Started                               | 24                    | 15                                       | 15                        |
| Received >/=1 Dose of Study Treatment | 19                    | 15                                       | 15                        |
| Completed                             | 0                     | 0                                        | 0                         |
| Not completed                         | 24                    | 15                                       | 15                        |

|                              |    |    |    |
|------------------------------|----|----|----|
| Adverse event, serious fatal | 18 | 15 | 15 |
| Consent withdrawn by subject | 3  | -  | -  |
| Physician decision           | 1  | -  | -  |
| Study Terminated By Sponsor  | 1  | -  | -  |
| Lost to follow-up            | 1  | -  | -  |

| Number of subjects in period 1        | Atezolizumab +<br>Selicrelumab +<br>Bevacizumab | Atezolizumab +<br>Idasanutlin | Atezolizumab +<br>Regorafenib |
|---------------------------------------|-------------------------------------------------|-------------------------------|-------------------------------|
|                                       |                                                 |                               |                               |
| Started                               | 6                                               | 4                             | 15                            |
| Received >/=1 Dose of Study Treatment | 6                                               | 4                             | 15                            |
| Completed                             | 0                                               | 0                             | 0                             |
| Not completed                         | 6                                               | 4                             | 15                            |
| Adverse event, serious fatal          | 4                                               | 4                             | 11                            |
| Consent withdrawn by subject          | 2                                               | -                             | 1                             |
| Physician decision                    | -                                               | -                             | -                             |
| Study Terminated By Sponsor           | -                                               | -                             | 2                             |
| Lost to follow-up                     | -                                               | -                             | 1                             |

| Number of subjects in period 1        | Atezolizumab +<br>Regorafenib +<br>AB928 | Atezolizumab +<br>LOAd703 |
|---------------------------------------|------------------------------------------|---------------------------|
|                                       |                                          |                           |
| Started                               | 15                                       | 2                         |
| Received >/=1 Dose of Study Treatment | 15                                       | 2                         |
| Completed                             | 0                                        | 0                         |
| Not completed                         | 15                                       | 2                         |
| Adverse event, serious fatal          | 12                                       | 1                         |
| Consent withdrawn by subject          | -                                        | -                         |
| Physician decision                    | -                                        | -                         |
| Study Terminated By Sponsor           | 3                                        | 1                         |
| Lost to follow-up                     | -                                        | -                         |

## Baseline characteristics

| Reporting groups                                                                                                                                                                                                                                |                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| Reporting group title                                                                                                                                                                                                                           | Regorafenib (Control)                     |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.                                                   |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Imprime PGG + Bevacizumab  |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Isatuximab                 |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Selicrelumab + Bevacizumab |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Idasanutlin                |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Regorafenib                |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Regorafenib + AB928        |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + LOAd703                    |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |

| Reporting group values                      | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab |
|---------------------------------------------|-----------------------|------------------------------------------|---------------------------|
| Number of subjects                          | 24                    | 15                                       | 15                        |
| Age Categorical<br>Units: Participants      |                       |                                          |                           |
| Preterm newborn (gestational age <37 weeks) | 0                     | 0                                        | 0                         |
| Newborns (0-27 days)                        | 0                     | 0                                        | 0                         |
| Infants and toddlers (28 days-23 months)    | 0                     | 0                                        | 0                         |
| Children (2-11 years)                       | 0                     | 0                                        | 0                         |
| Adults (18-64 years)                        | 17                    | 13                                       | 12                        |
| From 65-84 years                            | 7                     | 2                                        | 3                         |
| 85 years and over                           | 0                     | 0                                        | 0                         |

|                                                                                                                                                                                                                                           |                |               |                |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------------|----------------|
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation                                                                                                                                                                   | 59.5<br>± 10.3 | 57.8<br>± 5.9 | 52.3<br>± 12.0 |
| Sex: Female, Male<br>Units:                                                                                                                                                                                                               |                |               |                |
| Female                                                                                                                                                                                                                                    | 12             | 7             | 6              |
| Male                                                                                                                                                                                                                                      | 12             | 8             | 9              |
| Ethnicity (NIH/OMB)<br>Units: Subjects                                                                                                                                                                                                    |                |               |                |
| Hispanic or Latino                                                                                                                                                                                                                        | 2              | 4             | 3              |
| Not Hispanic or Latino                                                                                                                                                                                                                    | 21             | 10            | 11             |
| Unknown or Not Reported                                                                                                                                                                                                                   | 1              | 1             | 1              |
| Race (NIH/OMB)<br>Units: Subjects                                                                                                                                                                                                         |                |               |                |
| American Indian or Alaska Native                                                                                                                                                                                                          | 0              | 1             | 0              |
| Asian                                                                                                                                                                                                                                     | 7              | 6             | 4              |
| Native Hawaiian or Other Pacific Islander                                                                                                                                                                                                 | 0              | 0             | 0              |
| Black or African American                                                                                                                                                                                                                 | 1              | 0             | 0              |
| White                                                                                                                                                                                                                                     | 15             | 7             | 10             |
| More than one race                                                                                                                                                                                                                        | 0              | 1             | 0              |
| Unknown or Not Reported                                                                                                                                                                                                                   | 1              | 0             | 1              |
| ECOG score                                                                                                                                                                                                                                |                |               |                |
| ECOG performance status scale. 0 - Fully active; able to carry on all predisease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature |                |               |                |
| Units: Subjects                                                                                                                                                                                                                           |                |               |                |
| ECOG PS 0                                                                                                                                                                                                                                 | 11             | 8             | 5              |
| ECOG PS 1                                                                                                                                                                                                                                 | 13             | 7             | 10             |
| Number of Metastatic Sites at Enrollment<br>Units: Subjects                                                                                                                                                                               |                |               |                |
| 1 Site                                                                                                                                                                                                                                    | 3              | 1             | 0              |
| 2 Sites                                                                                                                                                                                                                                   | 4              | 5             | 3              |
| 3 Sites                                                                                                                                                                                                                                   | 9              | 5             | 8              |
| >/=4 Sites                                                                                                                                                                                                                                | 8              | 4             | 4              |

| Reporting group values                      | Atezolizumab +<br>Selicrelumab +<br>Bevacizumab | Atezolizumab +<br>Idasanutlin | Atezolizumab +<br>Regorafenib |
|---------------------------------------------|-------------------------------------------------|-------------------------------|-------------------------------|
| Number of subjects                          | 6                                               | 4                             | 15                            |
| Age Categorical<br>Units: Participants      |                                                 |                               |                               |
| Preterm newborn (gestational age <37 weeks) | 0                                               | 0                             | 0                             |
| Newborns (0-27 days)                        | 0                                               | 0                             | 0                             |
| Infants and toddlers (28 days-23 months)    | 0                                               | 0                             | 0                             |
| Children (2-11 years)                       | 0                                               | 0                             | 0                             |
| Adults (18-64 years)                        | 1                                               | 3                             | 12                            |
| From 65-84 years                            | 5                                               | 1                             | 3                             |
| 85 years and over                           | 0                                               | 0                             | 0                             |

|                                                                                                                                                                                                                                           |                |               |               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------------|---------------|
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation                                                                                                                                                                   | 66.8<br>± 10.0 | 56.3<br>± 6.8 | 56.4<br>± 8.2 |
| Sex: Female, Male<br>Units:                                                                                                                                                                                                               |                |               |               |
| Female                                                                                                                                                                                                                                    | 1              | 3             | 11            |
| Male                                                                                                                                                                                                                                      | 5              | 1             | 4             |
| Ethnicity (NIH/OMB)<br>Units: Subjects                                                                                                                                                                                                    |                |               |               |
| Hispanic or Latino                                                                                                                                                                                                                        | 1              | 0             | 1             |
| Not Hispanic or Latino                                                                                                                                                                                                                    | 4              | 4             | 11            |
| Unknown or Not Reported                                                                                                                                                                                                                   | 1              | 0             | 3             |
| Race (NIH/OMB)<br>Units: Subjects                                                                                                                                                                                                         |                |               |               |
| American Indian or Alaska Native                                                                                                                                                                                                          | 0              | 0             | 0             |
| Asian                                                                                                                                                                                                                                     | 0              | 1             | 5             |
| Native Hawaiian or Other Pacific Islander                                                                                                                                                                                                 | 0              | 0             | 0             |
| Black or African American                                                                                                                                                                                                                 | 0              | 0             | 1             |
| White                                                                                                                                                                                                                                     | 5              | 3             | 7             |
| More than one race                                                                                                                                                                                                                        | 0              | 0             | 0             |
| Unknown or Not Reported                                                                                                                                                                                                                   | 1              | 0             | 2             |
| ECOG score                                                                                                                                                                                                                                |                |               |               |
| ECOG performance status scale. 0 - Fully active; able to carry on all predisease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature |                |               |               |
| Units: Subjects                                                                                                                                                                                                                           |                |               |               |
| ECOG PS 0                                                                                                                                                                                                                                 | 5              | 1             | 7             |
| ECOG PS 1                                                                                                                                                                                                                                 | 1              | 3             | 8             |
| Number of Metastatic Sites at Enrollment<br>Units: Subjects                                                                                                                                                                               |                |               |               |
| 1 Site                                                                                                                                                                                                                                    | 0              | 0             | 1             |
| 2 Sites                                                                                                                                                                                                                                   | 3              | 3             | 7             |
| 3 Sites                                                                                                                                                                                                                                   | 0              | 0             | 2             |
| >/=4 Sites                                                                                                                                                                                                                                | 3              | 1             | 5             |

| Reporting group values                      | Atezolizumab +<br>Regorafenib +<br>AB928 | Atezolizumab +<br>LOAd703 | Total |
|---------------------------------------------|------------------------------------------|---------------------------|-------|
| Number of subjects                          | 15                                       | 2                         | 96    |
| Age Categorical<br>Units: Participants      |                                          |                           |       |
| Preterm newborn (gestational age <37 weeks) | 0                                        | 0                         | 0     |
| Newborns (0-27 days)                        | 0                                        | 0                         | 0     |
| Infants and toddlers (28 days-23 months)    | 0                                        | 0                         | 0     |
| Children (2-11 years)                       | 0                                        | 0                         | 0     |
| Adults (18-64 years)                        | 13                                       | 1                         | 72    |
| From 65-84 years                            | 2                                        | 1                         | 24    |
| 85 years and over                           | 0                                        | 0                         | 0     |

|                                                                                                                                                                                                                                           |               |                |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|----------------|----|
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation                                                                                                                                                                   | 55.1<br>± 9.2 | 58.0<br>± 11.3 | -  |
| Sex: Female, Male<br>Units:                                                                                                                                                                                                               |               |                |    |
| Female                                                                                                                                                                                                                                    | 4             | 1              | 45 |
| Male                                                                                                                                                                                                                                      | 11            | 1              | 51 |
| Ethnicity (NIH/OMB)<br>Units: Subjects                                                                                                                                                                                                    |               |                |    |
| Hispanic or Latino                                                                                                                                                                                                                        | 0             | 1              | 12 |
| Not Hispanic or Latino                                                                                                                                                                                                                    | 14            | 1              | 76 |
| Unknown or Not Reported                                                                                                                                                                                                                   | 1             | 0              | 8  |
| Race (NIH/OMB)<br>Units: Subjects                                                                                                                                                                                                         |               |                |    |
| American Indian or Alaska Native                                                                                                                                                                                                          | 0             | 0              | 1  |
| Asian                                                                                                                                                                                                                                     | 8             | 0              | 31 |
| Native Hawaiian or Other Pacific Islander                                                                                                                                                                                                 | 0             | 0              | 0  |
| Black or African American                                                                                                                                                                                                                 | 0             | 0              | 2  |
| White                                                                                                                                                                                                                                     | 6             | 2              | 55 |
| More than one race                                                                                                                                                                                                                        | 0             | 0              | 1  |
| Unknown or Not Reported                                                                                                                                                                                                                   | 1             | 0              | 6  |
| ECOG score                                                                                                                                                                                                                                |               |                |    |
| ECOG performance status scale. 0 - Fully active; able to carry on all predisease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature |               |                |    |
| Units: Subjects                                                                                                                                                                                                                           |               |                |    |
| ECOG PS 0                                                                                                                                                                                                                                 | 7             | 1              | 45 |
| ECOG PS 1                                                                                                                                                                                                                                 | 8             | 1              | 51 |
| Number of Metastatic Sites at Enrollment<br>Units: Subjects                                                                                                                                                                               |               |                |    |
| 1 Site                                                                                                                                                                                                                                    | 1             | 0              | 6  |
| 2 Sites                                                                                                                                                                                                                                   | 5             | 0              | 30 |
| 3 Sites                                                                                                                                                                                                                                   | 6             | 2              | 32 |
| >/=4 Sites                                                                                                                                                                                                                                | 3             | 0              | 28 |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                 |                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| Reporting group title                                                                                                                                                                                                                           | Regorafenib (Control)                     |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.                                                   |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Imprime PGG + Bevacizumab  |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Isatuximab                 |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Selicrelumab + Bevacizumab |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Idasanutlin                |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Regorafenib                |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + Regorafenib + AB928        |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |
| Reporting group title                                                                                                                                                                                                                           | Atezolizumab + LOAd703                    |
| Reporting group description:<br>Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator. |                                           |

### Primary: Best Confirmed Overall Response Rate (ORR) as Determined by the Investigator According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Best Confirmed Overall Response Rate (ORR) as Determined by the Investigator According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 |
| End point description:<br>The best confirmed ORR is defined as the percentage of participants with a complete response or partial response on two consecutive occasions $\geq 4$ weeks apart, as determined by the investigator according to RECIST v1.1. Participants could be classified as "Stable Disease" if the assessment was $\geq 6$ weeks from randomization. They were classified as Missing if no post-baseline response assessments were available, or as Not Evaluable if all post-baseline response assessments were unevaluable. The differences in ORR between the experimental arms and the corresponding control arm were calculated, along with 95% confidence intervals (CIs), using normal approximation of the binomial distribution. The 95% CIs for ORRs were constructed using the Clopper-Pearson method, and 0 to 999999 indicates that they were not calculated for the "Not Evaluable" and "Missing" categories. The 95% CIs for the difference in rates were constructed using the Wald method with continuity correction. |                                                                                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Primary                                                                                                                                              |

End point timeframe:

From randomization until disease progression or loss of clinical benefit (up to 4 years)

| End point values                  | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|-----------------------------------|-----------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type                | Reporting group       | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed       | 19                    | 15                                       | 15                        | 6                                         |
| Units: Percentage of Participants |                       |                                          |                           |                                           |
| number (confidence interval 95%)  |                       |                                          |                           |                                           |
| Responders (CR + PR)              | 0 (0 to 17.65)        | 0 (0 to 21.80)                           | 0 (0 to 21.80)            | 0 (0 to 45.93)                            |
| Complete Response (CR)            | 0 (0 to 17.65)        | 0 (0 to 21.80)                           | 0 (0 to 21.80)            | 0 (0 to 45.93)                            |
| Partial Response (PR)             | 0 (0 to 17.65)        | 0 (0 to 21.80)                           | 0 (0 to 21.80)            | 0 (0 to 45.93)                            |
| Stable Disease (SD)               | 63.2 (38.36 to 83.71) | 33.3 (11.82 to 61.62)                    | 20.0 (4.33 to 48.09)      | 50 (11.81 to 88.19)                       |
| Progressive Disease (PD)          | 26.3 (9.15 to 51.20)  | 66.7 (38.38 to 88.18)                    | 66.7 (38.38 to 88.18)     | 33.3 (4.33 to 77.72)                      |
| Not Evaluable                     | 0 (0 to 999999)       | 0 (0 to 999999)                          | 13.3 (0 to 999999)        | 0 (0 to 999999)                           |
| Missing                           | 10.5 (0 to 999999)    | 0 (0 to 999999)                          | 0 (0 to 999999)           | 16.7 (0 to 999999)                        |

| End point values                  | Atezolizumab + Idasanutlin | Atezolizumab + Regorafenib | Atezolizumab + Regorafenib + AB928 | Atezolizumab + LOAd703 |
|-----------------------------------|----------------------------|----------------------------|------------------------------------|------------------------|
| Subject group type                | Reporting group            | Reporting group            | Reporting group                    | Reporting group        |
| Number of subjects analysed       | 4                          | 15                         | 15                                 | 2                      |
| Units: Percentage of Participants |                            |                            |                                    |                        |
| number (confidence interval 95%)  |                            |                            |                                    |                        |
| Responders (CR + PR)              | 0 (0 to 60.24)             | 6.7 (0.17 to 31.95)        | 6.7 (0.17 to 31.95)                | 0 (0 to 84.19)         |
| Complete Response (CR)            | 0 (0 to 60.24)             | 0 (0 to 21.80)             | 0 (0 to 21.80)                     | 0 (0 to 84.19)         |
| Partial Response (PR)             | 0 (0 to 60.24)             | 6.7 (0.17 to 31.95)        | 6.7 (0.17 to 31.95)                | 0 (0 to 84.19)         |
| Stable Disease (SD)               | 0 (0 to 60.24)             | 33.3 (11.82 to 61.62)      | 53.3 (26.59 to 78.73)              | 0 (0 to 84.19)         |
| Progressive Disease (PD)          | 100 (39.76 to 100)         | 46.7 (21.27 to 73.41)      | 26.7 (7.79 to 55.10)               | 100 (15.81 to 100)     |
| Not Evaluable                     | 0 (0 to 999999)            | 0 (0 to 999999)            | 13.3 (0 to 999999)                 | 0 (0 to 999999)        |
| Missing                           | 0 (0 to 999999)            | 13.3 (0 to 999999)         | 0 (0 to 999999)                    | 0 (0 to 999999)        |

## Statistical analyses

|                            |                                                    |
|----------------------------|----------------------------------------------------|
| Statistical analysis title | The difference in ORR between arms                 |
| Comparison groups          | Regorafenib (Control) v Atezolizumab + Regorafenib |

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| Number of subjects included in analysis | 34                                  |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           |                                     |
| Parameter estimate                      | Difference in Overall Response Rate |
| Point estimate                          | 6.67                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -11.92                              |
| upper limit                             | 25.25                               |

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>       | The difference in ORR between arms                         |
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           |                                                            |
| Parameter estimate                      | Difference in Overall Response Rate                        |
| Point estimate                          | 6.67                                                       |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | -11.92                                                     |
| upper limit                             | 25.25                                                      |

## Secondary: Progression-Free Survival (PFS) as Determined by Investigator According to RECIST v1.1

|                 |                                                                                        |
|-----------------|----------------------------------------------------------------------------------------|
| End point title | Progression-Free Survival (PFS) as Determined by Investigator According to RECIST v1.1 |
|-----------------|----------------------------------------------------------------------------------------|

End point description:

Progression-free survival (PFS) after randomization, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), was determined by the investigator according to RECIST v1.1. For participants who did not have documented disease progression or death, PFS was censored at the day of the last tumor assessment. The Kaplan-Meier method was used to estimate the median for PFS with 95% confidence intervals (CIs) constructed through use of the Brookmeyer and Crowley method. The values "999999" indicate that the 95% CI could not be calculated because too few events had occurred.

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

End point timeframe:

From randomization up to the first occurrence of disease or death from any cause (up to 4 years)

| End point values                 | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|----------------------------------|-----------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type               | Reporting group       | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed      | 19                    | 15                                       | 15                        | 6                                         |
| Units: Months                    |                       |                                          |                           |                                           |
| median (confidence interval 95%) | 2.83 (2.20 to 3.02)   | 1.51 (1.38 to 2.79)                      | 1.41 (1.41 to 1.77)       | 4.21 (1.68 to 999999)                     |

| End point values                 | Atezolizumab + Idasanutlin | Atezolizumab + Regorafenib | Atezolizumab + Regorafenib + AB928 | Atezolizumab + LOAd703 |
|----------------------------------|----------------------------|----------------------------|------------------------------------|------------------------|
| Subject group type               | Reporting group            | Reporting group            | Reporting group                    | Reporting group        |
| Number of subjects analysed      | 4                          | 15                         | 15                                 | 2                      |
| Units: Months                    |                            |                            |                                    |                        |
| median (confidence interval 95%) | 1.26 (0.82 to 999999)      | 1.81 (1.38 to 2.96)        | 4.60 (2.60 to 5.78)                | 1.58 (1.51 to 999999)  |

## Statistical analyses

| Statistical analysis title              | PFS Hazard Ratio                                                 |
|-----------------------------------------|------------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab |
| Number of subjects included in analysis | 34                                                               |
| Analysis specification                  | Pre-specified                                                    |
| Analysis type                           | other                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                |
| Point estimate                          | 1.35                                                             |
| Confidence interval                     |                                                                  |
| level                                   | 95 %                                                             |
| sides                                   | 2-sided                                                          |
| lower limit                             | 0.67                                                             |
| upper limit                             | 2.73                                                             |

| Statistical analysis title              | PFS Hazard Ratio                                  |
|-----------------------------------------|---------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Isatuximab |
| Number of subjects included in analysis | 34                                                |
| Analysis specification                  | Pre-specified                                     |
| Analysis type                           | other                                             |
| Parameter estimate                      | Hazard ratio (HR)                                 |
| Point estimate                          | 2.3                                               |
| Confidence interval                     |                                                   |
| level                                   | 95 %                                              |
| sides                                   | 2-sided                                           |
| lower limit                             | 1.08                                              |
| upper limit                             | 4.88                                              |

|                                         |                                                                   |
|-----------------------------------------|-------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | PFS Hazard Ratio                                                  |
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab |
| Number of subjects included in analysis | 25                                                                |
| Analysis specification                  | Pre-specified                                                     |
| Analysis type                           | other                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                 |
| Point estimate                          | 0.79                                                              |
| Confidence interval                     |                                                                   |
| level                                   | 95 %                                                              |
| sides                                   | 2-sided                                                           |
| lower limit                             | 0.29                                                              |
| upper limit                             | 2.18                                                              |

|                                         |                                                |
|-----------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>       | PFS Hazard Ratio                               |
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + LOAd703 |
| Number of subjects included in analysis | 21                                             |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | other                                          |
| Parameter estimate                      | Hazard ratio (HR)                              |
| Point estimate                          | 5.64                                           |
| Confidence interval                     |                                                |
| level                                   | 95 %                                           |
| sides                                   | 2-sided                                        |
| lower limit                             | 0.94                                           |
| upper limit                             | 33.82                                          |

|                                         |                                                    |
|-----------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>       | PFS Hazard Ratio                                   |
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib |
| Number of subjects included in analysis | 34                                                 |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other                                              |
| Parameter estimate                      | Hazard ratio (HR)                                  |
| Point estimate                          | 1.74                                               |
| Confidence interval                     |                                                    |
| level                                   | 95 %                                               |
| sides                                   | 2-sided                                            |
| lower limit                             | 0.83                                               |
| upper limit                             | 3.63                                               |

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>       | PFS Hazard Ratio                                           |
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           | other                                                      |
| Parameter estimate                      | Hazard ratio (HR)                                          |
| Point estimate                          | 0.8                                                        |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | 0.39                                                       |
| upper limit                             | 1.63                                                       |

|                                         |                                                    |
|-----------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>       | PFS Hazard Ratio                                   |
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Idasanutlin |
| Number of subjects included in analysis | 23                                                 |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other                                              |
| Parameter estimate                      | Hazard ratio (HR)                                  |
| Point estimate                          | 2                                                  |
| Confidence interval                     |                                                    |
| level                                   | 95 %                                               |
| sides                                   | 2-sided                                            |
| lower limit                             | 0.64                                               |
| upper limit                             | 6.24                                               |

## Secondary: Overall Survival (OS)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Overall Survival (OS) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                       |
| Overall survival (OS) is defined as the time from randomization to death from any cause. Participants who were still alive at the time of OS analysis were censored at the last date they were known to be alive. The Kaplan-Meier method was used to estimate the median for OS with 95% confidence intervals (CIs) constructed through use of the Brookmeyer and Crowley method. The values "999999" indicate that the median or the 95% CI could not be calculated because too few events had occurred. |                       |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Secondary             |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                       |
| From randomization up to death from any cause (up to 4 years)                                                                                                                                                                                                                                                                                                                                                                                                                                              |                       |

| End point values                 | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|----------------------------------|-----------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type               | Reporting group       | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed      | 19                    | 15                                       | 15                        | 6                                         |
| Units: Months                    |                       |                                          |                           |                                           |
| median (confidence interval 95%) | 10.15 (4.40 to        | 5.72 (4.37 to                            | 5.13 (3.12 to             | 14.36 (3.22 to                            |

|        |        |       |         |
|--------|--------|-------|---------|
| 12.29) | 10.51) | 7.75) | 999999) |
|--------|--------|-------|---------|

| End point values                 | Atezolizumab +<br>Idasanutlin | Atezolizumab +<br>Regorafenib | Atezolizumab +<br>Regorafenib +<br>AB928 | Atezolizumab +<br>LOAd703    |
|----------------------------------|-------------------------------|-------------------------------|------------------------------------------|------------------------------|
| Subject group type               | Reporting group               | Reporting group               | Reporting group                          | Reporting group              |
| Number of subjects analysed      | 4                             | 15                            | 15                                       | 2                            |
| Units: Months                    |                               |                               |                                          |                              |
| median (confidence interval 95%) | 5.93 (1.61 to<br>999999)      | 11.01 (5.29 to<br>16.66)      | 8.67 (6.60 to<br>14.62)                  | 4.07 (0.999999<br>to 999999) |

## Statistical analyses

| Statistical analysis title                                                                                                  | OS Hazard Ratio                                                  |
|-----------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| Statistical analysis description:<br>Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) Hazard Ratio for OS |                                                                  |
| Comparison groups                                                                                                           | Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab |
| Number of subjects included in analysis                                                                                     | 34                                                               |
| Analysis specification                                                                                                      | Pre-specified                                                    |
| Analysis type                                                                                                               | other                                                            |
| Parameter estimate                                                                                                          | Hazard ratio (HR)                                                |
| Point estimate                                                                                                              | 1.44                                                             |
| Confidence interval                                                                                                         |                                                                  |
| level                                                                                                                       | 95 %                                                             |
| sides                                                                                                                       | 2-sided                                                          |
| lower limit                                                                                                                 | 0.71                                                             |
| upper limit                                                                                                                 | 2.93                                                             |

| Statistical analysis title                                                                                   | OS Hazard Ratio                                   |
|--------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Statistical analysis description:<br>Atezolizumab + Isatuximab vs. Regorafenib (Control) Hazard Ratio for OS |                                                   |
| Comparison groups                                                                                            | Regorafenib (Control) v Atezolizumab + Isatuximab |
| Number of subjects included in analysis                                                                      | 34                                                |
| Analysis specification                                                                                       | Pre-specified                                     |
| Analysis type                                                                                                | other                                             |
| Parameter estimate                                                                                           | Hazard ratio (HR)                                 |
| Point estimate                                                                                               | 1.38                                              |
| Confidence interval                                                                                          |                                                   |
| level                                                                                                        | 95 %                                              |
| sides                                                                                                        | 2-sided                                           |
| lower limit                                                                                                  | 0.68                                              |
| upper limit                                                                                                  | 2.81                                              |

|                                                                                                                              |                                                                   |
|------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                            | OS Hazard Ratio                                                   |
| Statistical analysis description:<br>Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) Hazard Ratio for OS |                                                                   |
| Comparison groups                                                                                                            | Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab |
| Number of subjects included in analysis                                                                                      | 25                                                                |
| Analysis specification                                                                                                       | Pre-specified                                                     |
| Analysis type                                                                                                                | other                                                             |
| Parameter estimate                                                                                                           | Hazard ratio (HR)                                                 |
| Point estimate                                                                                                               | 0.9                                                               |
| Confidence interval                                                                                                          |                                                                   |
| level                                                                                                                        | 95 %                                                              |
| sides                                                                                                                        | 2-sided                                                           |
| lower limit                                                                                                                  | 0.3                                                               |
| upper limit                                                                                                                  | 2.72                                                              |

|                                                                                                               |                                                    |
|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>                                                                             | OS Hazard Ratio                                    |
| Statistical analysis description:<br>Atezolizumab + Idasanutlin vs. Regorafenib (Control) Hazard Ratio for OS |                                                    |
| Comparison groups                                                                                             | Regorafenib (Control) v Atezolizumab + Idasanutlin |
| Number of subjects included in analysis                                                                       | 23                                                 |
| Analysis specification                                                                                        | Pre-specified                                      |
| Analysis type                                                                                                 | other                                              |
| Parameter estimate                                                                                            | Hazard ratio (HR)                                  |
| Point estimate                                                                                                | 1.27                                               |
| Confidence interval                                                                                           |                                                    |
| level                                                                                                         | 95 %                                               |
| sides                                                                                                         | 2-sided                                            |
| lower limit                                                                                                   | 0.42                                               |
| upper limit                                                                                                   | 3.84                                               |

|                                                                                                               |                                                    |
|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>                                                                             | OS Hazard Ratio                                    |
| Statistical analysis description:<br>Atezolizumab + Regorafenib vs. Regorafenib (Control) Hazard Ratio for OS |                                                    |
| Comparison groups                                                                                             | Regorafenib (Control) v Atezolizumab + Regorafenib |
| Number of subjects included in analysis                                                                       | 34                                                 |
| Analysis specification                                                                                        | Pre-specified                                      |
| Analysis type                                                                                                 | other                                              |
| Parameter estimate                                                                                            | Hazard ratio (HR)                                  |
| Point estimate                                                                                                | 0.86                                               |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.39    |
| upper limit         | 1.88    |

|                                                                                  |                                                            |
|----------------------------------------------------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                | OS Hazard Ratio                                            |
| Statistical analysis description:                                                |                                                            |
| Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) Hazard Ratio for OS |                                                            |
| Comparison groups                                                                | Atezolizumab + Regorafenib + AB928 v Regorafenib (Control) |
| Number of subjects included in analysis                                          | 34                                                         |
| Analysis specification                                                           | Pre-specified                                              |
| Analysis type                                                                    | other                                                      |
| Parameter estimate                                                               | Hazard ratio (HR)                                          |
| Point estimate                                                                   | 0.92                                                       |
| Confidence interval                                                              |                                                            |
| level                                                                            | 95 %                                                       |
| sides                                                                            | 2-sided                                                    |
| lower limit                                                                      | 0.43                                                       |
| upper limit                                                                      | 1.96                                                       |

|                                                                      |                                                |
|----------------------------------------------------------------------|------------------------------------------------|
| <b>Statistical analysis title</b>                                    | OS Hazard Ratio                                |
| Statistical analysis description:                                    |                                                |
| Atezolizumab + LOAd703 vs. Regorafenib (Control) Hazard Ratio for OS |                                                |
| Comparison groups                                                    | Regorafenib (Control) v Atezolizumab + LOAd703 |
| Number of subjects included in analysis                              | 21                                             |
| Analysis specification                                               | Pre-specified                                  |
| Analysis type                                                        | other                                          |
| Parameter estimate                                                   | Hazard ratio (HR)                              |
| Point estimate                                                       | 2.88                                           |
| Confidence interval                                                  |                                                |
| level                                                                | 95 %                                           |
| sides                                                                | 2-sided                                        |
| lower limit                                                          | 0.33                                           |
| upper limit                                                          | 24.85                                          |

## Secondary: Percentage of Participants Who Were Alive at Landmark Timepoints for Overall Survival (OS)

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants Who Were Alive at Landmark Timepoints for Overall Survival (OS) |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

Overall survival (OS) is defined as the time from randomization to death from any cause. Participants who were still alive at the time of OS analysis were censored at the last date they were known to be alive. OS is shown as the percentage of participants who were event-free at the landmark timepoints of 3, 6, 12, and 18 months. The values "999999" indicate that the 95% CI could not be calculated because

too few events had occurred.

|                         |           |
|-------------------------|-----------|
| End point type          | Secondary |
| End point timeframe:    |           |
| 3, 6, 12, and 18 months |           |

| End point values                  | Regorafenib (Control)   | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|-----------------------------------|-------------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type                | Reporting group         | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed       | 19                      | 15                                       | 15                        | 6                                         |
| Units: Percentage of Participants |                         |                                          |                           |                                           |
| number (confidence interval 95%)  |                         |                                          |                           |                                           |
| 3 Months                          | 84.21 (67.81 to 100.00) | 100 (100 to 100)                         | 73.33 (50.95 to 95.71)    | 100 (100 to 100)                          |
| 6 Months                          | 63.16 (41.47 to 84.85)  | 46.67 (21.42 to 71.91)                   | 40.00 (15.21 to 64.79)    | 80.00 (44.94 to 100)                      |
| 12 Months                         | 34.45 (12.42 to 56.48)  | 20.00 (0.00 to 40.24)                    | 26.67 (4.29 to 49.05)     | 53.33 (4.68 to 100)                       |
| 18 Months                         | 17.22 (0.00 to 34.87)   | 6.67 (0.00 to 19.29)                     | 20.00 (0.00 to 40.24)     | 26.67 (0.00 to 70.91)                     |

| End point values                  | Atezolizumab + Idasanutlin | Atezolizumab + Regorafenib | Atezolizumab + Regorafenib + AB928 | Atezolizumab + LOAd703 |
|-----------------------------------|----------------------------|----------------------------|------------------------------------|------------------------|
| Subject group type                | Reporting group            | Reporting group            | Reporting group                    | Reporting group        |
| Number of subjects analysed       | 4                          | 15                         | 15                                 | 2                      |
| Units: Percentage of Participants |                            |                            |                                    |                        |
| number (confidence interval 95%)  |                            |                            |                                    |                        |
| 3 Months                          | 75.00 (32.57 to 100)       | 78.97 (57.78 to 100.00)    | 86.67 (69.46 to 100.00)            | 100 (100 to 100)       |
| 6 Months                          | 50.00 (1.00 to 99.00)      | 71.79 (48.32 to 95.27)     | 73.33 (50.95 to 95.71)             | 0 (0 to 999999)        |
| 12 Months                         | 25.00 (0.00 to 67.43)      | 39.89 (13.18 to 66.59)     | 33.33 (9.48 to 57.19)              | 0 (0 to 999999)        |
| 18 Months                         | 25.00 (0.00 to 67.43)      | 23.93 (0.48 to 47.39)      | 26.67 (4.29 to 49.05)              | 0 (0 to 999999)        |

## Statistical analyses

|                                                                                                                              |                                                                  |
|------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| Statistical analysis title                                                                                                   | Difference in OS Event-Free Rate                                 |
| Statistical analysis description:                                                                                            |                                                                  |
| Difference in OS event-free rate at 6 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms |                                                                  |
| Comparison groups                                                                                                            | Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab |

|                                         |                                  |
|-----------------------------------------|----------------------------------|
| Number of subjects included in analysis | 34                               |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | other                            |
| Parameter estimate                      | Difference in OS Event-Free Rate |
| Point estimate                          | -16.49                           |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -49.78                           |
| upper limit                             | 16.79                            |

|                                                                                                                              |                                                                  |
|------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                            | Difference in OS Event-Free Rate                                 |
| Statistical analysis description:                                                                                            |                                                                  |
| Difference in OS event-free rate at 3 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms |                                                                  |
| Comparison groups                                                                                                            | Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab |
| Number of subjects included in analysis                                                                                      | 34                                                               |
| Analysis specification                                                                                                       | Pre-specified                                                    |
| Analysis type                                                                                                                | other                                                            |
| Parameter estimate                                                                                                           | Difference in OS Event-Free Rate                                 |
| Point estimate                                                                                                               | 15.79                                                            |
| Confidence interval                                                                                                          |                                                                  |
| level                                                                                                                        | 95 %                                                             |
| sides                                                                                                                        | 2-sided                                                          |
| lower limit                                                                                                                  | -0.61                                                            |
| upper limit                                                                                                                  | 32.19                                                            |

|                                                                                                               |                                                   |
|---------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| <b>Statistical analysis title</b>                                                                             | Difference in OS Event-Free Rate                  |
| Statistical analysis description:                                                                             |                                                   |
| Difference in OS event-free rate at 3 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms |                                                   |
| Comparison groups                                                                                             | Regorafenib (Control) v Atezolizumab + Isatuximab |
| Number of subjects included in analysis                                                                       | 34                                                |
| Analysis specification                                                                                        | Pre-specified                                     |
| Analysis type                                                                                                 | other                                             |
| Parameter estimate                                                                                            | Difference in OS Event-Free Rate                  |
| Point estimate                                                                                                | -10.88                                            |
| Confidence interval                                                                                           |                                                   |
| level                                                                                                         | 95 %                                              |
| sides                                                                                                         | 2-sided                                           |
| lower limit                                                                                                   | -38.62                                            |
| upper limit                                                                                                   | 16.87                                             |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

---

**Statistical analysis description:**

Difference in OS event-free rate at 18 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms

|                                         |                                                                  |
|-----------------------------------------|------------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab |
| Number of subjects included in analysis | 34                                                               |
| Analysis specification                  | Pre-specified                                                    |
| Analysis type                           | other                                                            |
| Parameter estimate                      | Difference in OS Event-Free Rate                                 |
| Point estimate                          | -10.56                                                           |
| Confidence interval                     |                                                                  |
| level                                   | 95 %                                                             |
| sides                                   | 2-sided                                                          |
| lower limit                             | -32.25                                                           |
| upper limit                             | 11.14                                                            |

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**Statistical analysis title**

Difference in OS Event-Free Rate

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**Statistical analysis description:**

Difference in OS event-free rate at 12 months for the Atezolizumab + Imprime PGG + Bevacizumab vs. Regorafenib (Control) arms

|                                         |                                                                  |
|-----------------------------------------|------------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Imprime PGG + Bevacizumab |
| Number of subjects included in analysis | 34                                                               |
| Analysis specification                  | Pre-specified                                                    |
| Analysis type                           | other                                                            |
| Parameter estimate                      | Difference in OS Event-Free Rate                                 |
| Point estimate                          | -14.45                                                           |
| Confidence interval                     |                                                                  |
| level                                   | 95 %                                                             |
| sides                                   | 2-sided                                                          |
| lower limit                             | -44.37                                                           |
| upper limit                             | 15.47                                                            |

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**Statistical analysis title**

Difference in OS Event-Free Rate

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**Statistical analysis description:**

Difference in OS event-free rate at 12 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms

|                                         |                                                                   |
|-----------------------------------------|-------------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab |
| Number of subjects included in analysis | 25                                                                |
| Analysis specification                  | Pre-specified                                                     |
| Analysis type                           | other                                                             |
| Parameter estimate                      | Difference in OS Event-Free Rate                                  |
| Point estimate                          | 18.88                                                             |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -34.53  |
| upper limit         | 72.3    |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 18 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms

|                                         |                                                                   |
|-----------------------------------------|-------------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab |
| Number of subjects included in analysis | 25                                                                |
| Analysis specification                  | Pre-specified                                                     |
| Analysis type                           | other                                                             |
| Parameter estimate                      | Difference in OS Event-Free Rate                                  |
| Point estimate                          | 9.44                                                              |
| Confidence interval                     |                                                                   |
| level                                   | 95 %                                                              |
| sides                                   | 2-sided                                                           |
| lower limit                             | -38.19                                                            |
| upper limit                             | 57.08                                                             |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 6 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms

|                                         |                                                                   |
|-----------------------------------------|-------------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab |
| Number of subjects included in analysis | 25                                                                |
| Analysis specification                  | Pre-specified                                                     |
| Analysis type                           | other                                                             |
| Parameter estimate                      | Difference in OS Event-Free Rate                                  |
| Point estimate                          | 16.84                                                             |
| Confidence interval                     |                                                                   |
| level                                   | 95 %                                                              |
| sides                                   | 2-sided                                                           |
| lower limit                             | -24.39                                                            |
| upper limit                             | 58.07                                                             |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 3 months for the Atezolizumab + Selicrelumab + Bevacizumab vs. Regorafenib (Control) arms

|                   |                                                                   |
|-------------------|-------------------------------------------------------------------|
| Comparison groups | Regorafenib (Control) v Atezolizumab + Selicrelumab + Bevacizumab |
|-------------------|-------------------------------------------------------------------|

|                                         |                                  |
|-----------------------------------------|----------------------------------|
| Number of subjects included in analysis | 25                               |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | other                            |
| Parameter estimate                      | Difference in OS Event-Free Rate |
| Point estimate                          | 15.79                            |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -0.61                            |
| upper limit                             | 32.19                            |

|                                                                                                                                                     |                                                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                   | Difference in OS Event-Free Rate                  |
| Statistical analysis description:<br>Difference in OS event-free rate at 18 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms |                                                   |
| Comparison groups                                                                                                                                   | Regorafenib (Control) v Atezolizumab + Isatuximab |
| Number of subjects included in analysis                                                                                                             | 34                                                |
| Analysis specification                                                                                                                              | Pre-specified                                     |
| Analysis type                                                                                                                                       | other                                             |
| Parameter estimate                                                                                                                                  | Difference in OS Event-Free Rate                  |
| Point estimate                                                                                                                                      | 2.78                                              |
| Confidence interval                                                                                                                                 |                                                   |
| level                                                                                                                                               | 95 %                                              |
| sides                                                                                                                                               | 2-sided                                           |
| lower limit                                                                                                                                         | -24.08                                            |
| upper limit                                                                                                                                         | 29.63                                             |

|                                                                                                                                                     |                                                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                   | Difference in OS Event-Free Rate                  |
| Statistical analysis description:<br>Difference in OS event-free rate at 12 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms |                                                   |
| Comparison groups                                                                                                                                   | Regorafenib (Control) v Atezolizumab + Isatuximab |
| Number of subjects included in analysis                                                                                                             | 34                                                |
| Analysis specification                                                                                                                              | Pre-specified                                     |
| Analysis type                                                                                                                                       | other                                             |
| Parameter estimate                                                                                                                                  | Difference in OS Event-Free Rate                  |
| Point estimate                                                                                                                                      | -7.78                                             |
| Confidence interval                                                                                                                                 |                                                   |
| level                                                                                                                                               | 95 %                                              |
| sides                                                                                                                                               | 2-sided                                           |
| lower limit                                                                                                                                         | -39.19                                            |
| upper limit                                                                                                                                         | 23.62                                             |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

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**Statistical analysis description:**

Difference in OS event-free rate at 6 months for the Atezolizumab + Isatuximab vs. Regorafenib (Control) arms

|                                         |                                                   |
|-----------------------------------------|---------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Isatuximab |
| Number of subjects included in analysis | 34                                                |
| Analysis specification                  | Pre-specified                                     |
| Analysis type                           | other                                             |
| Parameter estimate                      | Difference in OS Event-Free Rate                  |
| Point estimate                          | -23.16                                            |
| Confidence interval                     |                                                   |
| level                                   | 95 %                                              |
| sides                                   | 2-sided                                           |
| lower limit                             | -56.1                                             |
| upper limit                             | 9.78                                              |

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**Statistical analysis title**

Difference in OS Event-Free Rate

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**Statistical analysis description:**

Difference in OS event-free rate at 3 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms

|                                         |                                                    |
|-----------------------------------------|----------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Idasanutlin |
| Number of subjects included in analysis | 23                                                 |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other                                              |
| Parameter estimate                      | Difference in OS Event-Free Rate                   |
| Point estimate                          | -9.21                                              |
| Confidence interval                     |                                                    |
| level                                   | 95 %                                               |
| sides                                   | 2-sided                                            |
| lower limit                             | -54.7                                              |
| upper limit                             | 36.28                                              |

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**Statistical analysis title**

Difference in OS Event-Free Rate

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**Statistical analysis description:**

Difference in OS event-free rate at 3 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms

|                                         |                                                    |
|-----------------------------------------|----------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib |
| Number of subjects included in analysis | 34                                                 |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other                                              |
| Parameter estimate                      | Difference in OS Event-Free Rate                   |
| Point estimate                          | -5.24                                              |
| Confidence interval                     |                                                    |
| level                                   | 95 %                                               |
| sides                                   | 2-sided                                            |
| lower limit                             | -32.03                                             |
| upper limit                             | 21.56                                              |

|                                                                                                                 |                                                    |
|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>                                                                               | Difference in OS Event-Free Rate                   |
| Statistical analysis description:                                                                               |                                                    |
| Difference in OS event-free rate at 18 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms |                                                    |
| Comparison groups                                                                                               | Regorafenib (Control) v Atezolizumab + Idasanutlin |
| Number of subjects included in analysis                                                                         | 23                                                 |
| Analysis specification                                                                                          | Pre-specified                                      |
| Analysis type                                                                                                   | other                                              |
| Parameter estimate                                                                                              | Difference in OS Event-Free Rate                   |
| Point estimate                                                                                                  | 7.78                                               |
| Confidence interval                                                                                             |                                                    |
| level                                                                                                           | 95 %                                               |
| sides                                                                                                           | 2-sided                                            |
| lower limit                                                                                                     | -38.18                                             |
| upper limit                                                                                                     | 53.73                                              |

|                                                                                                                 |                                                    |
|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>                                                                               | Difference in OS Event-Free Rate                   |
| Statistical analysis description:                                                                               |                                                    |
| Difference in OS event-free rate at 12 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms |                                                    |
| Comparison groups                                                                                               | Regorafenib (Control) v Atezolizumab + Idasanutlin |
| Number of subjects included in analysis                                                                         | 23                                                 |
| Analysis specification                                                                                          | Pre-specified                                      |
| Analysis type                                                                                                   | other                                              |
| Parameter estimate                                                                                              | Difference in OS Event-Free Rate                   |
| Point estimate                                                                                                  | -9.45                                              |
| Confidence interval                                                                                             |                                                    |
| level                                                                                                           | 95 %                                               |
| sides                                                                                                           | 2-sided                                            |
| lower limit                                                                                                     | -57.26                                             |
| upper limit                                                                                                     | 38.36                                              |

|                                                                                                                |                                                    |
|----------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b>                                                                              | Difference in OS Event-Free Rate                   |
| Statistical analysis description:                                                                              |                                                    |
| Difference in OS event-free rate at 6 months for the Atezolizumab + Idasanutlin vs. Regorafenib (Control) arms |                                                    |
| Comparison groups                                                                                              | Regorafenib (Control) v Atezolizumab + Idasanutlin |
| Number of subjects included in analysis                                                                        | 23                                                 |
| Analysis specification                                                                                         | Pre-specified                                      |
| Analysis type                                                                                                  | other                                              |
| Parameter estimate                                                                                             | Difference in OS Event-Free Rate                   |
| Point estimate                                                                                                 | -13.16                                             |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -66.74  |
| upper limit         | 40.43   |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 6 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms

|                                         |                                                    |
|-----------------------------------------|----------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib |
| Number of subjects included in analysis | 34                                                 |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other                                              |
| Parameter estimate                      | Difference in OS Event-Free Rate                   |
| Point estimate                          | 8.64                                               |
| Confidence interval                     |                                                    |
| level                                   | 95 %                                               |
| sides                                   | 2-sided                                            |
| lower limit                             | -23.33                                             |
| upper limit                             | 40.6                                               |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 12 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           | other                                                      |
| Parameter estimate                      | Difference in OS Event-Free Rate                           |
| Point estimate                          | 5.44                                                       |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | -29.19                                                     |
| upper limit                             | 40.06                                                      |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 18 months for the Atezolizumab + Regorafenib vs. Regorafenib (Control) arms

|                   |                                                    |
|-------------------|----------------------------------------------------|
| Comparison groups | Regorafenib (Control) v Atezolizumab + Regorafenib |
|-------------------|----------------------------------------------------|

|                                         |                                  |
|-----------------------------------------|----------------------------------|
| Number of subjects included in analysis | 34                               |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | other                            |
| Parameter estimate                      | Difference in OS Event-Free Rate |
| Point estimate                          | 6.71                             |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -22.64                           |
| upper limit                             | 36.06                            |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 18 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           | other                                                      |
| Parameter estimate                      | Difference in OS Event-Free Rate                           |
| Point estimate                          | 9.44                                                       |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | -19.06                                                     |
| upper limit                             | 37.94                                                      |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Difference in OS event-free rate at 12 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           | other                                                      |
| Parameter estimate                      | Difference in OS Event-Free Rate                           |
| Point estimate                          | -1.12                                                      |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | -33.59                                                     |
| upper limit                             | 31.36                                                      |

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Difference in OS Event-Free Rate |
|-----------------------------------|----------------------------------|

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**Statistical analysis description:**

Difference in OS event-free rate at 6 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           | other                                                      |
| Parameter estimate                      | Difference in OS Event-Free Rate                           |
| Point estimate                          | 10.18                                                      |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | -20.99                                                     |
| upper limit                             | 41.34                                                      |

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**Statistical analysis title**

Difference in OS Event-Free Rate

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**Statistical analysis description:**

Difference in OS event-free rate at 3 months for the Atezolizumab + Regorafenib + AB928 vs. Regorafenib (Control) arms

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + Regorafenib + AB928 |
| Number of subjects included in analysis | 34                                                         |
| Analysis specification                  | Pre-specified                                              |
| Analysis type                           | other                                                      |
| Parameter estimate                      | Difference in OS Event-Free Rate                           |
| Point estimate                          | 2.46                                                       |
| Confidence interval                     |                                                            |
| level                                   | 95 %                                                       |
| sides                                   | 2-sided                                                    |
| lower limit                             | -21.31                                                     |
| upper limit                             | 26.22                                                      |

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**Statistical analysis title**

Difference in OS Event-Free Rate

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**Statistical analysis description:**

Difference in OS event-free rate at 3 months for the Atezolizumab + LOAd703 vs. Regorafenib (Control) arms

|                                         |                                                |
|-----------------------------------------|------------------------------------------------|
| Comparison groups                       | Regorafenib (Control) v Atezolizumab + LOAd703 |
| Number of subjects included in analysis | 21                                             |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | other                                          |
| Parameter estimate                      | Difference in OS Event-Free Rate               |
| Point estimate                          | 15.79                                          |
| Confidence interval                     |                                                |
| level                                   | 95 %                                           |
| sides                                   | 2-sided                                        |
| lower limit                             | -0.61                                          |
| upper limit                             | 32.19                                          |

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**Secondary: Duration of Response (DOR) as Determined by the Investigator According to RECIST v1.1**

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|                 |                                                                                       |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Duration of Response (DOR) as Determined by the Investigator According to RECIST v1.1 |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

Duration of response is defined as the time from the first occurrence of a documented objective response to disease progression or death from any cause, whichever occurs first. In both arms where DOR was measured only 1 participant had a confirmed response; 95% CI could not be calculated.

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

End point timeframe:

From the date of first occurrence of a documented objective response to disease progression or death from any cause, whichever occurs first (up to 4 years)

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| End point values                 | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|----------------------------------|-----------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type               | Reporting group       | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed      | 0 <sup>[1]</sup>      | 0 <sup>[2]</sup>                         | 0 <sup>[3]</sup>          | 0 <sup>[4]</sup>                          |
| Units: Months                    |                       |                                          |                           |                                           |
| median (confidence interval 95%) | ( to )                | ( to )                                   | ( to )                    | ( to )                                    |

Notes:

[1] - None of the patients in this arm had a confirmed response.

[2] - None of the patients in this arm had a confirmed response.

[3] - None of the patients in this arm had a confirmed response.

[4] - None of the patients in this arm had a confirmed response.

| End point values                 | Atezolizumab + Idasanutlin | Atezolizumab + Regorafenib | Atezolizumab + Regorafenib + AB928 | Atezolizumab + LOAd703 |
|----------------------------------|----------------------------|----------------------------|------------------------------------|------------------------|
| Subject group type               | Reporting group            | Reporting group            | Reporting group                    | Reporting group        |
| Number of subjects analysed      | 0 <sup>[5]</sup>           | 1 <sup>[6]</sup>           | 1 <sup>[7]</sup>                   | 0 <sup>[8]</sup>       |
| Units: Months                    |                            |                            |                                    |                        |
| median (confidence interval 95%) | ( to )                     | 3.12 (0 to 999999)         | 5.75 (0 to 999999)                 | ( to )                 |

Notes:

[5] - None of the patients in this arm had a confirmed response.

[6] - 1 patient with a confirmed response; 95% CI could not be calculated.

[7] - 1 patient with a confirmed response; 95% CI could not be calculated.

[8] - None of the patients in this arm had a confirmed response.

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Disease Control Rate (DCR), as Determined by the Investigator per RECIST v1.1**

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|                 |                                                                               |
|-----------------|-------------------------------------------------------------------------------|
| End point title | Disease Control Rate (DCR), as Determined by the Investigator per RECIST v1.1 |
|-----------------|-------------------------------------------------------------------------------|

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End point description:

Disease control rate is defined as the percentage of participants with stable disease for  $\geq 12$  weeks or a complete or partial response, as determined by the investigator according to RECIST v1.1.

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

End point timeframe:

From randomization until disease progression or loss of clinical benefit (up to 4 years)

| End point values                  | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|-----------------------------------|-----------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type                | Reporting group       | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed       | 19                    | 15                                       | 15                        | 6                                         |
| Units: Percentage of Participants |                       |                                          |                           |                                           |
| number (confidence interval 95%)  | 15.8 (3.38 to 39.58)  | 13.3 (1.66 to 40.46)                     | 6.7 (0.17 to 31.95)       | 33.3 (4.33 to 77.72)                      |

| End point values                  | Atezolizumab + Idasanutlin | Atezolizumab + Regorafenib | Atezolizumab + Regorafenib + AB928 | Atezolizumab + LOAd703 |
|-----------------------------------|----------------------------|----------------------------|------------------------------------|------------------------|
| Subject group type                | Reporting group            | Reporting group            | Reporting group                    | Reporting group        |
| Number of subjects analysed       | 4                          | 15                         | 15                                 | 2                      |
| Units: Percentage of Participants |                            |                            |                                    |                        |
| number (confidence interval 95%)  | 0 (0.00 to 60.24)          | 13.3 (1.66 to 40.46)       | 40.0 (16.34 to 67.71)              | 0 (0.00 to 84.19)      |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with at Least One Adverse Event (AE)

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Percentage of Participants with at Least One Adverse Event (AE) |
|-----------------|-----------------------------------------------------------------|

End point description:

The incidence, nature, and severity of adverse events (AEs) are reported, with severity determined according to NCI CTCAE v4.0. AEs were reported for the safety-evaluable population, which included all patients who received any amount of dose of any component of study treatment. All AEs were reported until 30 days after the last study dose or until start of new systemic anti-cancer therapy. Serious AEs and AEs of special interest were reported until 135 days (or 180 days for the Atezolizumab + LOAd703 arm only) after the last dose of study treatment.

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

End point timeframe:

Adverse event data were collected from baseline up to 6 months after the last dose of study treatment (up to 640 days); deaths (all-cause) were reported from baseline through survival follow-up (up to 4 years)

| End point values                                 | Regorafenib (Control) | Atezolizumab + Imprime PGG + Bevacizumab | Atezolizumab + Isatuximab | Atezolizumab + Selicrelumab + Bevacizumab |
|--------------------------------------------------|-----------------------|------------------------------------------|---------------------------|-------------------------------------------|
| Subject group type                               | Reporting group       | Reporting group                          | Reporting group           | Reporting group                           |
| Number of subjects analysed                      | 19                    | 15                                       | 15                        | 6                                         |
| Units: Percentage of Participants                |                       |                                          |                           |                                           |
| number (not applicable)                          |                       |                                          |                           |                                           |
| Adverse Event (AE)                               | 100                   | 100                                      | 100                       | 100                                       |
| Death                                            | 89.5                  | 100                                      | 100                       | 66.7                                      |
| Withdrawn from Stage due to an AE                | 15.8                  | 6.7                                      | 0                         | 0                                         |
| AE with a Fatal Outcome                          | 10.5                  | 0                                        | 0                         | 0                                         |
| Serious AE (SAE)                                 | 26.3                  | 6.7                                      | 33.3                      | 50.0                                      |
| SAE Leading to Withdrawal from any Treatment     | 21.1                  | 6.7                                      | 0                         | 0                                         |
| SAE Leading to Dose Modification/Interruption    | 5.3                   | 0                                        | 6.7                       | 50.0                                      |
| Related SAE                                      | 5.3                   | 6.7                                      | 0                         | 50.0                                      |
| AE Leading to Withdrawal from any Treatment      | 26.3                  | 6.7                                      | 0                         | 0                                         |
| AE Leading to Dose Modification/Interruption     | 63.2                  | 40.0                                     | 13.3                      | 50.0                                      |
| Related AE                                       | 94.7                  | 86.7                                     | 86.7                      | 100                                       |
| Related AE Leading to Withdrawal from Treatment  | 10.5                  | 6.7                                      | 0                         | 0                                         |
| Related AE Leading to Dose Modified/Interruption | 47.4                  | 33.3                                     | 0                         | 33.3                                      |
| Grade 3-5 AE                                     | 68.4                  | 20.0                                     | 46.7                      | 50.0                                      |
| Worst Grade AE: 5                                | 10.5                  | 0                                        | 0                         | 0                                         |
| Worst Grade AE: 4                                | 5.3                   | 0                                        | 6.7                       | 0                                         |
| Worst Grade AE: 3                                | 52.6                  | 20.0                                     | 40.0                      | 50.0                                      |

| End point values                              | Atezolizumab + Idasanutlin | Atezolizumab + Regorafenib | Atezolizumab + Regorafenib + AB928 | Atezolizumab + LOAd703 |
|-----------------------------------------------|----------------------------|----------------------------|------------------------------------|------------------------|
| Subject group type                            | Reporting group            | Reporting group            | Reporting group                    | Reporting group        |
| Number of subjects analysed                   | 4                          | 15                         | 15                                 | 2                      |
| Units: Percentage of Participants             |                            |                            |                                    |                        |
| number (not applicable)                       |                            |                            |                                    |                        |
| Adverse Event (AE)                            | 100                        | 100                        | 100                                | 100                    |
| Death                                         | 100                        | 73.3                       | 80.0                               | 50.0                   |
| Withdrawn from Stage due to an AE             | 0                          | 6.7                        | 6.7                                | 0                      |
| AE with a Fatal Outcome                       | 0                          | 6.7                        | 0                                  | 0                      |
| Serious AE (SAE)                              | 25.0                       | 46.7                       | 46.7                               | 50.0                   |
| SAE Leading to Withdrawal from any Treatment  | 0                          | 6.7                        | 0                                  | 0                      |
| SAE Leading to Dose Modification/Interruption | 0                          | 26.7                       | 46.7                               | 0                      |
| Related SAE                                   | 25.0                       | 26.7                       | 33.3                               | 50.0                   |
| AE Leading to Withdrawal from any Treatment   | 0                          | 20.0                       | 6.7                                | 0                      |
| AE Leading to Dose Modification/Interruption  | 75.0                       | 86.7                       | 93.3                               | 0                      |
| Related AE                                    | 100                        | 93.3                       | 100                                | 50.0                   |

|                                                  |      |      |      |   |
|--------------------------------------------------|------|------|------|---|
| Related AE Leading to Withdrawal from Treatment  | 0    | 6.7  | 6.7  | 0 |
| Related AE Leading to Dose Modified/Interruption | 75.0 | 73.3 | 93.3 | 0 |
| Grade 3-5 AE                                     | 75.0 | 66.7 | 60.0 | 0 |
| Worst Grade AE: 5                                | 0    | 6.7  | 0    | 0 |
| Worst Grade AE: 4                                | 25.0 | 6.7  | 13.3 | 0 |
| Worst Grade AE: 3                                | 50.0 | 53.3 | 46.7 | 0 |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data were collected from baseline up to 6 months after the last dose of study treatment (up to 640 days); the total number of deaths (all-cause) reported include survival follow-up (up to 4 years)

Adverse event reporting additional description:

AEs were reported for the safety population, defined as all those who received  $\geq 1$  dose of study treatment. All AEs were reported until 30 days after the last study dose or until start of new systemic anti-cancer therapy. Serious AEs and AEs of special interest were reported until 135 days (180 days for Atezo + LOAd703) after the last study dose.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |                                           |
|-----------------------|-------------------------------------------|
| Reporting group title | Atezolizumab + Selicrelumab + Bevacizumab |
|-----------------------|-------------------------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | Atezolizumab + Isatuximab |
|-----------------------|---------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Regorafenib (Control) |
|-----------------------|-----------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.

|                       |                                          |
|-----------------------|------------------------------------------|
| Reporting group title | Atezolizumab + Imprime PGG + Bevacizumab |
|-----------------------|------------------------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Atezolizumab + Idasanutlin |
|-----------------------|----------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | Atezolizumab + Regorafenib + AB928 |
|-----------------------|------------------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Atezolizumab + Regorafenib |
|-----------------------|----------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Atezolizumab + LOAd703 |
|-----------------------|------------------------|

Reporting group description:

Participants will receive treatment until unacceptable toxicity or loss of clinical benefit as confirmed by disease progression per RECIST V1.1 or lack of continued benefit as determined by the investigator.

| Serious adverse events                                              | Atezolizumab +<br>Selicrelumab +<br>Bevacizumab | Atezolizumab +<br>Isatuximab | Regorafenib<br>(Control) |
|---------------------------------------------------------------------|-------------------------------------------------|------------------------------|--------------------------|
| Total subjects affected by serious adverse events                   |                                                 |                              |                          |
| subjects affected / exposed                                         | 3 / 6 (50.00%)                                  | 5 / 15 (33.33%)              | 5 / 19 (26.32%)          |
| number of deaths (all causes)                                       | 4                                               | 15                           | 17                       |
| number of deaths resulting from adverse events                      |                                                 |                              |                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                 |                              |                          |
| Tumour haemorrhage                                                  |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 0 / 19 (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                    |
| Vascular disorders                                                  |                                                 |                              |                          |
| Hypertension                                                        |                                                 |                              |                          |
| subjects affected / exposed                                         | 1 / 6 (16.67%)                                  | 0 / 15 (0.00%)               | 0 / 19 (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                    |
| General disorders and administration site conditions                |                                                 |                              |                          |
| Asthenia                                                            |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 0 / 19 (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                    |
| Perforation                                                         |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 0 / 19 (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                    |
| Pyrexia                                                             |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 0 / 19 (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                    |
| Immune system disorders                                             |                                                 |                              |                          |
| Cytokine release syndrome                                           |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 0 / 19 (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                    |
| Hypersensitivity                                                    |                                                 |                              |                          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Dyspnoea                                        |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Epistaxis                                       |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (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          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (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          |
| Respiratory failure                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 19 (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          |
| Haemoptysis                                     |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 15 (6.67%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypoxia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Investigations                                  |                |                |                |
| Blood bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Injury, poisoning and procedural complications  |                |                |                |
| Lumbar vertebral fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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 disorders                               |                |                |                |
| Atrial flutter                                  |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (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          |
| Nervous system disorders                        |                |                |                |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (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          |
| Blood and lymphatic system disorders            |                |                |                |
| Febrile neutropenia                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Leukocytosis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Thrombocytopenia                                |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Thrombotic microangiopathy                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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                      |                |                |                |
| Abdominal pain                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Large intestinal obstruction                    |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 19 (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          |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (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          |
| Nausea                                          |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Vomiting                                        |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Small intestinal obstruction                    |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 15 (6.67%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Biliary obstruction                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Rash                                            |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (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          |
| Rash maculo-papular                             |                |                |                |

|                                                 |               |                |                 |
|-------------------------------------------------|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 19 (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           |
| Musculoskeletal and connective tissue disorders |               |                |                 |
| Fistula                                         |               |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 19 (5.26%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Infections and infestations                     |               |                |                 |
| Bacteraemia                                     |               |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 19 (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           |
| Biliary tract infection                         |               |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 19 (5.26%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Urinary tract infection                         |               |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 19 (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 / 6 (0.00%) | 1 / 15 (6.67%) | 2 / 19 (10.53%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 2           |
| Pyelonephritis                                  |               |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 19 (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           |
| Enterocolitis infectious                        |               |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 19 (5.26%)  |
| 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                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 19 (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          |

| <b>Serious adverse events</b>                                       | Atezolizumab +<br>Imprime PGG +<br>Bevacizumab | Atezolizumab +<br>Idasanutlin | Atezolizumab +<br>Regorafenib +<br>AB928 |
|---------------------------------------------------------------------|------------------------------------------------|-------------------------------|------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                |                               |                                          |
| subjects affected / exposed                                         | 1 / 15 (6.67%)                                 | 1 / 4 (25.00%)                | 7 / 15 (46.67%)                          |
| number of deaths (all causes)                                       | 15                                             | 4                             | 12                                       |
| number of deaths resulting from adverse events                      |                                                |                               |                                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                |                               |                                          |
| Tumour haemorrhage                                                  |                                                |                               |                                          |
| subjects affected / exposed                                         | 0 / 15 (0.00%)                                 | 0 / 4 (0.00%)                 | 0 / 15 (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                                    |
| Vascular disorders                                                  |                                                |                               |                                          |
| Hypertension                                                        |                                                |                               |                                          |
| subjects affected / exposed                                         | 0 / 15 (0.00%)                                 | 0 / 4 (0.00%)                 | 0 / 15 (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                                    |
| General disorders and administration site conditions                |                                                |                               |                                          |
| Asthenia                                                            |                                                |                               |                                          |
| subjects affected / exposed                                         | 0 / 15 (0.00%)                                 | 0 / 4 (0.00%)                 | 1 / 15 (6.67%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                          | 0 / 0                         | 1 / 1                                    |
| deaths causally related to treatment / all                          | 0 / 0                                          | 0 / 0                         | 0 / 0                                    |
| Perforation                                                         |                                                |                               |                                          |
| subjects affected / exposed                                         | 1 / 15 (6.67%)                                 | 0 / 4 (0.00%)                 | 0 / 15 (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                                    |
| Pyrexia                                                             |                                                |                               |                                          |
| subjects affected / exposed                                         | 0 / 15 (0.00%)                                 | 0 / 4 (0.00%)                 | 2 / 15 (13.33%)                          |
| occurrences causally related to treatment / all                     | 0 / 0                                          | 0 / 0                         | 1 / 2                                    |
| deaths causally related to treatment / all                          | 0 / 0                                          | 0 / 0                         | 0 / 0                                    |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| Immune system disorders                         |                |               |                |
| Cytokine release syndrome                       |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Hypersensitivity                                |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |               |                |
| Dyspnoea                                        |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Epistaxis                                       |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Pneumothorax                                    |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Respiratory failure                             |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Haemoptysis                                     |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Hypoxia                                         |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Investigations                                  |                |                |                |
| Blood bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (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          |
| Injury, poisoning and procedural complications  |                |                |                |
| Lumbar vertebral fracture                       |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 1 / 15 (6.67%) |
| 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                               |                |                |                |
| Atrial flutter                                  |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (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                        |                |                |                |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (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          |
| Blood and lymphatic system disorders            |                |                |                |
| Febrile neutropenia                             |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Leukocytosis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (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          |
| Thrombocytopenia                                |                |                |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 1 / 4 (25.00%) | 0 / 15 (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          |
| Thrombotic microangiopathy                      |                |                |                |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| <b>Gastrointestinal disorders</b>               |                |               |                |
| Abdominal pain                                  |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Large intestinal obstruction                    |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Diarrhoea                                       |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Nausea                                          |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Vomiting                                        |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Small intestinal obstruction                    |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| <b>Hepatobiliary disorders</b>                  |                |               |                |
| Biliary obstruction                             |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| <b>Skin and subcutaneous tissue disorders</b>   |                |               |                |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| Rash                                            |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Rash maculo-papular                             |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |               |                |
| Fistula                                         |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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                     |                |               |                |
| Bacteraemia                                     |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Biliary tract infection                         |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Urinary tract infection                         |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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 / 15 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pyelonephritis                                  |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| Enterocolitis infectious                        |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |
| Metabolism and nutrition disorders              |                |               |                |
| Dehydration                                     |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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          |

| <b>Serious adverse events</b>                                       | Atezolizumab + Regorafenib | Atezolizumab + LOAd703 |  |
|---------------------------------------------------------------------|----------------------------|------------------------|--|
| Total subjects affected by serious adverse events                   |                            |                        |  |
| subjects affected / exposed                                         | 7 / 15 (46.67%)            | 1 / 2 (50.00%)         |  |
| number of deaths (all causes)                                       | 11                         | 1                      |  |
| number of deaths resulting from adverse events                      |                            |                        |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                            |                        |  |
| Tumour haemorrhage                                                  |                            |                        |  |
| subjects affected / exposed                                         | 1 / 15 (6.67%)             | 0 / 2 (0.00%)          |  |
| occurrences causally related to treatment / all                     | 0 / 1                      | 0 / 0                  |  |
| deaths causally related to treatment / all                          | 0 / 1                      | 0 / 0                  |  |
| Vascular disorders                                                  |                            |                        |  |
| Hypertension                                                        |                            |                        |  |
| subjects affected / exposed                                         | 0 / 15 (0.00%)             | 0 / 2 (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                |                            |                        |  |
| Asthenia                                                            |                            |                        |  |
| subjects affected / exposed                                         | 0 / 15 (0.00%)             | 0 / 2 (0.00%)          |  |
| occurrences causally related to treatment / all                     | 0 / 0                      | 0 / 0                  |  |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                  |  |
| Perforation                                                         |                            |                        |  |
| subjects affected / exposed                                         | 0 / 15 (0.00%)             | 0 / 2 (0.00%)          |  |
| occurrences causally related to treatment / all                     | 0 / 0                      | 0 / 0                  |  |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                  |  |
| Pyrexia                                                             |                            |                        |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed                     | 3 / 15 (20.00%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 2 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Immune system disorders                         |                 |                |  |
| Cytokine release syndrome                       |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 1 / 2 (50.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypersensitivity                                |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 0 / 2 (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 |                 |                |  |
| Dyspnoea                                        |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Epistaxis                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumothorax                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory failure                             |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Haemoptysis                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|                                                 |                |               |  |
|-------------------------------------------------|----------------|---------------|--|
| Hypoxia                                         |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Investigations                                  |                |               |  |
| Blood bilirubin increased                       |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Injury, poisoning and procedural complications  |                |               |  |
| Lumbar vertebral fracture                       |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Cardiac disorders                               |                |               |  |
| Atrial flutter                                  |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Nervous system disorders                        |                |               |  |
| Syncope                                         |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (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            |                |               |  |
| Febrile neutropenia                             |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Leukocytosis                                    |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Thrombocytopenia                                |                |               |  |

|                                                 |                |               |  |
|-------------------------------------------------|----------------|---------------|--|
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Thrombotic microangiopathy                      |                |               |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Gastrointestinal disorders                      |                |               |  |
| Abdominal pain                                  |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Large intestinal obstruction                    |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Diarrhoea                                       |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Nausea                                          |                |               |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Vomiting                                        |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Small intestinal obstruction                    |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Hepatobiliary disorders                         |                |               |  |

|                                                 |                |               |  |
|-------------------------------------------------|----------------|---------------|--|
| Biliary obstruction                             |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Skin and subcutaneous tissue disorders          |                |               |  |
| Rash                                            |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Rash maculo-papular                             |                |               |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Musculoskeletal and connective tissue disorders |                |               |  |
| Fistula                                         |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Infections and infestations                     |                |               |  |
| Bacteraemia                                     |                |               |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Biliary tract infection                         |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (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                     | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Sepsis                                          |                |               |  |

|                                                 |                |               |  |
|-------------------------------------------------|----------------|---------------|--|
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (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                     | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Enterocolitis infectious                        |                |               |  |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 2 (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 / 15 (0.00%) | 0 / 2 (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>                                   | Atezolizumab +<br>Selicrelumab +<br>Bevacizumab | Atezolizumab +<br>Isatuximab | Regorafenib<br>(Control) |
|---------------------------------------------------------------------|-------------------------------------------------|------------------------------|--------------------------|
| Total subjects affected by non-serious adverse events               |                                                 |                              |                          |
| subjects affected / exposed                                         | 6 / 6 (100.00%)                                 | 15 / 15 (100.00%)            | 19 / 19 (100.00%)        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                 |                              |                          |
| Tumour fistulisation                                                |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 1 / 19 (5.26%)           |
| occurrences (all)                                                   | 0                                               | 0                            | 1                        |
| Tumour pain                                                         |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 1 / 19 (5.26%)           |
| occurrences (all)                                                   | 0                                               | 0                            | 1                        |
| Vascular disorders                                                  |                                                 |                              |                          |
| Vena cava thrombosis                                                |                                                 |                              |                          |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                   | 0 / 15 (0.00%)               | 1 / 19 (5.26%)           |
| occurrences (all)                                                   | 0                                               | 0                            | 1                        |
| Hypertension                                                        |                                                 |                              |                          |

|                                                         |                     |                     |                      |
|---------------------------------------------------------|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)        | 1 / 6 (16.67%)<br>5 | 1 / 15 (6.67%)<br>1 | 6 / 19 (31.58%)<br>7 |
| General disorders and administration<br>site conditions |                     |                     |                      |
| Asthenia                                                |                     |                     |                      |
| subjects affected / exposed                             | 2 / 6 (33.33%)      | 1 / 15 (6.67%)      | 2 / 19 (10.53%)      |
| occurrences (all)                                       | 3                   | 2                   | 2                    |
| Chest discomfort                                        |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                   | 0                    |
| Chest pain                                              |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 2 / 15 (13.33%)     | 3 / 19 (15.79%)      |
| occurrences (all)                                       | 0                   | 3                   | 3                    |
| Chills                                                  |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 4 / 15 (26.67%)     | 0 / 19 (0.00%)       |
| occurrences (all)                                       | 0                   | 6                   | 0                    |
| Inflammation                                            |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                   | 0                    |
| General physical health deterioration                   |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                   | 0                    |
| Non-cardiac chest pain                                  |                     |                     |                      |
| subjects affected / exposed                             | 1 / 6 (16.67%)      | 1 / 15 (6.67%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                       | 1                   | 1                   | 1                    |
| Mucosal inflammation                                    |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                       | 0                   | 0                   | 2                    |
| Medical device site erythema                            |                     |                     |                      |
| subjects affected / exposed                             | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                   | 0                    |
| Injection site reaction                                 |                     |                     |                      |
| subjects affected / exposed                             | 5 / 6 (83.33%)      | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                       | 9                   | 0                   | 0                    |
| Influenza like illness                                  |                     |                     |                      |

|                                         |                |                 |                 |
|-----------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed             | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0               |
| Device related thrombosis               |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Face oedema                             |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 0              | 1               | 0               |
| Fatigue                                 |                |                 |                 |
| subjects affected / exposed             | 2 / 6 (33.33%) | 9 / 15 (60.00%) | 8 / 19 (42.11%) |
| occurrences (all)                       | 2              | 11              | 8               |
| Oedema                                  |                |                 |                 |
| subjects affected / exposed             | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0               |
| Systemic inflammatory response syndrome |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Pyrexia                                 |                |                 |                 |
| subjects affected / exposed             | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 3 / 19 (15.79%) |
| occurrences (all)                       | 1              | 0               | 4               |
| Peripheral swelling                     |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Pain                                    |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 0              | 1               | 0               |
| Oedema peripheral                       |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 1 / 19 (5.26%)  |
| occurrences (all)                       | 0              | 1               | 1               |
| Swelling face                           |                |                 |                 |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Immune system disorders                 |                |                 |                 |
| Hypersensitivity                        |                |                 |                 |

|                                                 |                |                 |                 |
|-------------------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Cytokine release syndrome                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Reproductive system and breast disorders        |                |                 |                 |
| Intermenstrual bleeding                         |                |                 |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)                               | 0              | 0               | 1               |
| Perineal fistula                                |                |                 |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Vaginal haemorrhage                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Respiratory, thoracic and mediastinal disorders |                |                 |                 |
| Dyspnoea exertional                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Aspiration                                      |                |                 |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0               |
| Cough                                           |                |                 |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 4 / 15 (26.67%) | 2 / 19 (10.53%) |
| occurrences (all)                               | 1              | 5               | 2               |
| Dysphonia                                       |                |                 |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 5 / 19 (26.32%) |
| occurrences (all)                               | 1              | 0               | 7               |
| Dyspnoea                                        |                |                 |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 2 / 15 (13.33%) | 4 / 19 (21.05%) |
| occurrences (all)                               | 1              | 2               | 4               |
| Aphonia                                         |                |                 |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Epistaxis                                       |                |                 |                 |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| Haemoptysis                 |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Hypoxia                     |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Nasal congestion            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 15 (13.33%) | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 2               | 0              |
| Nasal dryness               |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Rhinorrhoea                 |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| Sinus congestion            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Wheezing                    |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Oropharyngeal pain          |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 15 (6.67%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 1              | 1               | 1              |
| Psychiatric disorders       |                |                 |                |
| Agitation                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)           | 0              | 0               | 1              |
| Anxiety                     |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 1              | 1               | 0              |
| Depression                  |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |

|                                                                                                 |                     |                      |                      |
|-------------------------------------------------------------------------------------------------|---------------------|----------------------|----------------------|
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                    | 2 / 6 (33.33%)<br>2 | 2 / 15 (13.33%)<br>2 | 3 / 19 (15.79%)<br>3 |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Product issues<br>Device occlusion<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Investigations<br>Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 4 / 19 (21.05%)<br>5 |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 2 / 19 (10.53%)<br>3 |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 1 / 19 (5.26%)<br>1  |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 3 / 19 (15.79%)<br>4 |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 4 / 19 (21.05%)<br>5 |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 2 / 19 (10.53%)<br>2 |

|                                                                                         |                     |                     |                      |
|-----------------------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)      | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Lymphocyte count increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 2 / 19 (10.53%)<br>2 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 2 / 19 (10.53%)<br>2 |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)    | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |
| Injury, poisoning and procedural complications                                          |                     |                     |                      |
| Intentional overdose<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1  |
| Injection related reaction<br>subjects affected / exposed<br>occurrences (all)          | 1 / 6 (16.67%)<br>2 | 0 / 15 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0  |
| Infusion related reaction                                                               |                     |                     |                      |

|                                   |                |                  |                |
|-----------------------------------|----------------|------------------|----------------|
| subjects affected / exposed       | 0 / 6 (0.00%)  | 11 / 15 (73.33%) | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 13               | 0              |
| Gastrointestinal anastomotic leak |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Facial bones fracture             |                |                  |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 15 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 1              | 0                | 0              |
| Corneal abrasion                  |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Accidental overdose               |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)                 | 0              | 0                | 1              |
| Stoma site rash                   |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Procedural pain                   |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)                 | 0              | 0                | 1              |
| Cardiac disorders                 |                |                  |                |
| Atrial fibrillation               |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 1 / 15 (6.67%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 1                | 0              |
| Palpitations                      |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 1 / 19 (5.26%) |
| occurrences (all)                 | 0              | 0                | 1              |
| Sinus tachycardia                 |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 0                | 0              |
| Tachycardia                       |                |                  |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 1 / 15 (6.67%)   | 0 / 19 (0.00%) |
| occurrences (all)                 | 0              | 1                | 0              |
| Nervous system disorders          |                |                  |                |
| Dizziness                         |                |                  |                |

|                                      |                |                 |                |
|--------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed          | 1 / 6 (16.67%) | 2 / 15 (13.33%) | 0 / 19 (0.00%) |
| occurrences (all)                    | 1              | 2               | 0              |
| Cerebellar syndrome                  |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Disturbance in attention             |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0              |
| Dysgeusia                            |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Headache                             |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                    | 0              | 0               | 1              |
| Hyperaesthesia                       |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                    | 0              | 0               | 1              |
| Myoclonus                            |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0              |
| Peripheral motor neuropathy          |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0              |
| Peripheral sensory neuropathy        |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 1 / 19 (5.26%) |
| occurrences (all)                    | 0              | 1               | 1              |
| Sciatica                             |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Syncope                              |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                    | 0              | 0               | 1              |
| Neuropathy peripheral                |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Blood and lymphatic system disorders |                |                 |                |

|                                                                                                        |                     |                      |                      |
|--------------------------------------------------------------------------------------------------------|---------------------|----------------------|----------------------|
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 2 / 19 (10.53%)<br>2 |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 6 (16.67%)<br>1 | 3 / 15 (20.00%)<br>3 | 2 / 19 (10.53%)<br>2 |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 2 / 19 (10.53%)<br>2 |
| Ear and labyrinth disorders<br>Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Ear discomfort<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 19 (0.00%)<br>0  |
| Eye disorders<br>Lacrimation increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 19 (0.00%)<br>0  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 19 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1  |
| Ascites<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 1 / 19 (5.26%)<br>3  |
| Anal haemorrhage                                                                                       |                     |                      |                      |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Abdominal pain upper        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Abdominal pain lower        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Abdominal pain              |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 4 / 15 (26.67%) | 5 / 19 (26.32%) |
| occurrences (all)           | 0              | 4               | 5               |
| Abdominal distension        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Colitis                     |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Dry mouth                   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 2 / 19 (10.53%) |
| occurrences (all)           | 0              | 0               | 2               |
| Diarrhoea                   |                |                 |                 |
| subjects affected / exposed | 2 / 6 (33.33%) | 2 / 15 (13.33%) | 6 / 19 (31.58%) |
| occurrences (all)           | 2              | 3               | 9               |
| Constipation                |                |                 |                 |
| subjects affected / exposed | 2 / 6 (33.33%) | 3 / 15 (20.00%) | 4 / 19 (21.05%) |
| occurrences (all)           | 2              | 3               | 4               |
| Dyspepsia                   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Odynophagia                 |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Nausea                      |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 6 / 15 (40.00%) | 7 / 19 (36.84%) |
| occurrences (all)           | 0              | 8               | 7               |
| Haemorrhoids                |                |                 |                 |

|                                  |                |                 |                |
|----------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                | 0              | 0               | 1              |
| Dysphagia                        |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 1               | 0              |
| Gastrooesophageal reflux disease |                |                 |                |
| subjects affected / exposed      | 1 / 6 (16.67%) | 1 / 15 (6.67%)  | 1 / 19 (5.26%) |
| occurrences (all)                | 1              | 1               | 1              |
| Frequent bowel movements         |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 1               | 0              |
| Enterocolitis                    |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Gingival bleeding                |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Vomiting                         |                |                 |                |
| subjects affected / exposed      | 1 / 6 (16.67%) | 3 / 15 (20.00%) | 1 / 19 (5.26%) |
| occurrences (all)                | 1              | 4               | 1              |
| Stomatitis                       |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                | 0              | 0               | 1              |
| Salivary duct inflammation       |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Rectal haemorrhage               |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Proctalgia                       |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                | 0              | 1               | 0              |
| Post-tussive vomiting            |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                | 0              | 0               | 1              |
| Oral pain                        |                |                 |                |

|                                                  |                     |                     |                      |
|--------------------------------------------------|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0 | 2 / 19 (10.53%)<br>2 |
| Hepatobiliary disorders                          |                     |                     |                      |
| Hyperbilirubinaemia                              |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 2 / 19 (10.53%)      |
| occurrences (all)                                | 0                   | 0                   | 2                    |
| Hepatic vein thrombosis                          |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Jaundice                                         |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                | 0                   | 0                   | 1                    |
| Skin and subcutaneous tissue disorders           |                     |                     |                      |
| Dermatitis acneiform                             |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 1 / 15 (6.67%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                | 0                   | 1                   | 0                    |
| Alopecia                                         |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 1 / 15 (6.67%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                | 0                   | 1                   | 1                    |
| Dry skin                                         |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                | 0                   | 0                   | 1                    |
| Erythema                                         |                     |                     |                      |
| subjects affected / exposed                      | 1 / 6 (16.67%)      | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Hair colour changes                              |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                | 0                   | 0                   | 1                    |
| Hyperhidrosis                                    |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 0 / 19 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Rash                                             |                     |                     |                      |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 15 (0.00%)      | 1 / 19 (5.26%)       |
| occurrences (all)                                | 0                   | 0                   | 1                    |
| Night sweats                                     |                     |                     |                      |

|                                             |                |                |                  |
|---------------------------------------------|----------------|----------------|------------------|
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |
| Palmar-plantar erythrodysaesthesia syndrome |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 12 / 19 (63.16%) |
| occurrences (all)                           | 0              | 0              | 18               |
| Pruritus                                    |                |                |                  |
| subjects affected / exposed                 | 1 / 6 (16.67%) | 1 / 15 (6.67%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 1              | 1              | 0                |
| Psoriasis                                   |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |
| Hyperkeratosis                              |                |                |                  |
| subjects affected / exposed                 | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 1 / 19 (5.26%)   |
| occurrences (all)                           | 1              | 0              | 1                |
| Rash macular                                |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |
| Rash maculo-papular                         |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |
| Rash papular                                |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |
| Seborrhoeic dermatitis                      |                |                |                  |
| subjects affected / exposed                 | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 1              | 0              | 0                |
| Urticaria                                   |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |
| Xeroderma                                   |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 19 (5.26%)   |
| occurrences (all)                           | 0              | 0              | 1                |
| Skin exfoliation                            |                |                |                  |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |

|                                                 |                |                |                 |
|-------------------------------------------------|----------------|----------------|-----------------|
| Renal and urinary disorders                     |                |                |                 |
| Urinary incontinence                            |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Dysuria                                         |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Haematuria                                      |                |                |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0               |
| Proteinuria                                     |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Renal pain                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Acute kidney injury                             |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Urinary retention                               |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 15 (6.67%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 1              | 1              | 0               |
| Endocrine disorders                             |                |                |                 |
| Hypothyroidism                                  |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 15 (6.67%) | 2 / 19 (10.53%) |
| occurrences (all)                               | 1              | 1              | 2               |
| Hyperthyroidism                                 |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Arthralgia                                      |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 15 (6.67%) | 1 / 19 (5.26%)  |
| occurrences (all)                               | 2              | 1              | 1               |
| Arthritis                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 19 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Groin pain                  |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Bone pain                   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Flank pain                  |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Fracture pain               |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Back pain                   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 1               | 1               |
| Muscle discomfort           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Muscle spasms               |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Musculoskeletal pain        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Myalgia                     |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 15 (13.33%) | 1 / 19 (5.26%)  |
| occurrences (all)           | 1              | 2               | 1               |
| Neck pain                   |                |                 |                 |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%)  |
| occurrences (all)           | 2              | 0               | 0               |
| Pain in extremity           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 5 / 19 (26.32%) |
| occurrences (all)           | 0              | 0               | 5               |
| Infections and infestations |                |                 |                 |
| Nasopharyngitis             |                |                 |                 |

|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 19 (5.26%) |
| occurrences (all)                  | 0              | 0               | 1              |
| Influenza                          |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 0               | 0              |
| Gingivitis                         |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 0               | 0              |
| Otitis media                       |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 0               | 0              |
| Sinusitis                          |                |                 |                |
| subjects affected / exposed        | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 3              | 0               | 0              |
| Sepsis                             |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 0               | 0              |
| Rash pustular                      |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 1               | 0              |
| Pneumonia                          |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 1 / 19 (5.26%) |
| occurrences (all)                  | 0              | 1               | 1              |
| Soft tissue infection              |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 0               | 0              |
| Tooth infection                    |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 0               | 0              |
| Urinary tract infection            |                |                 |                |
| subjects affected / exposed        | 1 / 6 (16.67%) | 2 / 15 (13.33%) | 1 / 19 (5.26%) |
| occurrences (all)                  | 2              | 2               | 1              |
| Upper respiratory tract infection  |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 3 / 15 (20.00%) | 0 / 19 (0.00%) |
| occurrences (all)                  | 0              | 3               | 0              |
| Metabolism and nutrition disorders |                |                 |                |

|                                                                              |                     |                      |                      |
|------------------------------------------------------------------------------|---------------------|----------------------|----------------------|
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)       | 2 / 6 (33.33%)<br>2 | 4 / 15 (26.67%)<br>4 | 6 / 19 (31.58%)<br>6 |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 19 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 19 (0.00%)<br>0  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)         | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1  |
| Malnutrition<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)             | 1 / 6 (16.67%)<br>1 | 2 / 15 (13.33%)<br>2 | 3 / 19 (15.79%)<br>3 |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)          | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)            | 1 / 6 (16.67%)<br>1 | 1 / 15 (6.67%)<br>1  | 2 / 19 (10.53%)<br>2 |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)        | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0  | 2 / 19 (10.53%)<br>2 |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 1 / 19 (5.26%)<br>1  |
| Type 2 diabetes mellitus<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0  |

|                                                                                                                                                    |                                                |                               |                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|-------------------------------|------------------------------------------|
| Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all)                                                                           | 0 / 6 (0.00%)<br>0                             | 0 / 15 (0.00%)<br>0           | 1 / 19 (5.26%)<br>1                      |
| <b>Non-serious adverse events</b>                                                                                                                  | Atezolizumab +<br>Imprime PGG +<br>Bevacizumab | Atezolizumab +<br>Idasanutlin | Atezolizumab +<br>Regorafenib +<br>AB928 |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                                            | 15 / 15 (100.00%)                              | 4 / 4 (100.00%)               | 15 / 15 (100.00%)                        |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>Tumour fistulisation<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0                            | 0 / 4 (0.00%)<br>0            | 0 / 15 (0.00%)<br>0                      |
| Tumour pain<br>subjects affected / exposed<br>occurrences (all)                                                                                    | 0 / 15 (0.00%)<br>0                            | 0 / 4 (0.00%)<br>0            | 1 / 15 (6.67%)<br>1                      |
| Vascular disorders<br>Vena cava thrombosis<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 15 (0.00%)<br>0                            | 0 / 4 (0.00%)<br>0            | 0 / 15 (0.00%)<br>0                      |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                                                                                   | 3 / 15 (20.00%)<br>3                           | 1 / 4 (25.00%)<br>1           | 3 / 15 (20.00%)<br>4                     |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 15 (0.00%)<br>0                            | 0 / 4 (0.00%)<br>0            | 2 / 15 (13.33%)<br>2                     |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)                                                                               | 0 / 15 (0.00%)<br>0                            | 1 / 4 (25.00%)<br>1           | 0 / 15 (0.00%)<br>0                      |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)                                                                                     | 2 / 15 (13.33%)<br>2                           | 0 / 4 (0.00%)<br>0            | 0 / 15 (0.00%)<br>0                      |
| Chills<br>subjects affected / exposed<br>occurrences (all)                                                                                         | 4 / 15 (26.67%)<br>4                           | 0 / 4 (0.00%)<br>0            | 1 / 15 (6.67%)<br>1                      |
| Inflammation                                                                                                                                       |                                                |                               |                                          |

|                                         |                 |                |                 |
|-----------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| General physical health deterioration   |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Non-cardiac chest pain                  |                 |                |                 |
| subjects affected / exposed             | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                       | 1               | 0              | 1               |
| Mucosal inflammation                    |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                       | 0               | 0              | 2               |
| Medical device site erythema            |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Injection site reaction                 |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Influenza like illness                  |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Device related thrombosis               |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                       | 0               | 0              | 1               |
| Face oedema                             |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Fatigue                                 |                 |                |                 |
| subjects affected / exposed             | 7 / 15 (46.67%) | 1 / 4 (25.00%) | 4 / 15 (26.67%) |
| occurrences (all)                       | 11              | 2              | 6               |
| Oedema                                  |                 |                |                 |
| subjects affected / exposed             | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                       | 1               | 0              | 0               |
| Systemic inflammatory response syndrome |                 |                |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                       | 0               | 1              | 0               |

|                                                                                                                            |                      |                    |                      |
|----------------------------------------------------------------------------------------------------------------------------|----------------------|--------------------|----------------------|
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                                                                | 4 / 15 (26.67%)<br>5 | 0 / 4 (0.00%)<br>0 | 7 / 15 (46.67%)<br>9 |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)                                                    | 1 / 15 (6.67%)<br>2  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                                                   | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Swelling face<br>subjects affected / exposed<br>occurrences (all)                                                          | 1 / 15 (6.67%)<br>1  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |
| Cytokine release syndrome<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Intermenstrual bleeding<br>subjects affected / exposed<br>occurrences (all)    | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Perineal fistula<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                                    | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| Aspiration                  |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Cough                       |                 |                |                 |
| subjects affected / exposed | 3 / 15 (20.00%) | 1 / 4 (25.00%) | 2 / 15 (13.33%) |
| occurrences (all)           | 4               | 1              | 2               |
| Dysphonia                   |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Dyspnoea                    |                 |                |                 |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 2               | 0              | 1               |
| Aphonia                     |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Epistaxis                   |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Haemoptysis                 |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Hypoxia                     |                 |                |                 |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Nasal congestion            |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Nasal dryness               |                 |                |                 |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Rhinorrhoea                 |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Sinus congestion            |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |

|                                                                                            |                      |                     |                      |
|--------------------------------------------------------------------------------------------|----------------------|---------------------|----------------------|
| Wheezing<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 2 / 15 (13.33%)<br>2 |
| Psychiatric disorders                                                                      |                      |                     |                      |
| Agitation<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 15 (13.33%)<br>2 | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Product issues                                                                             |                      |                     |                      |
| Device occlusion<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 15 (6.67%)<br>1  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Investigations                                                                             |                      |                     |                      |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)              | 1 / 15 (6.67%)<br>1  | 2 / 4 (50.00%)<br>2 | 3 / 15 (20.00%)<br>3 |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 3 / 15 (20.00%)<br>3 |

|                                       |                 |                |                 |
|---------------------------------------|-----------------|----------------|-----------------|
| Blood lactate dehydrogenase increased |                 |                |                 |
| subjects affected / exposed           | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 0               | 0              | 1               |
| C-reactive protein increased          |                 |                |                 |
| subjects affected / exposed           | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 0               | 0              | 1               |
| Aspartate aminotransferase increased  |                 |                |                 |
| subjects affected / exposed           | 2 / 15 (13.33%) | 2 / 4 (50.00%) | 3 / 15 (20.00%) |
| occurrences (all)                     | 2               | 2              | 3               |
| Alanine aminotransferase increased    |                 |                |                 |
| subjects affected / exposed           | 3 / 15 (20.00%) | 1 / 4 (25.00%) | 2 / 15 (13.33%) |
| occurrences (all)                     | 4               | 1              | 2               |
| Blood alkaline phosphatase increased  |                 |                |                 |
| subjects affected / exposed           | 2 / 15 (13.33%) | 1 / 4 (25.00%) | 2 / 15 (13.33%) |
| occurrences (all)                     | 2               | 1              | 2               |
| Electrocardiogram QT prolonged        |                 |                |                 |
| subjects affected / exposed           | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 0              | 0               |
| Gamma-glutamyltransferase increased   |                 |                |                 |
| subjects affected / exposed           | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                     | 0               | 0              | 2               |
| Lipase increased                      |                 |                |                 |
| subjects affected / exposed           | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 0               | 0              | 1               |
| Lymphocyte count decreased            |                 |                |                 |
| subjects affected / exposed           | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 1               | 0              | 1               |
| Lymphocyte count increased            |                 |                |                 |
| subjects affected / exposed           | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 1              | 0               |
| Neutrophil count decreased            |                 |                |                 |
| subjects affected / exposed           | 1 / 15 (6.67%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                     | 1               | 1              | 0               |
| Platelet count decreased              |                 |                |                 |

|                                                |                 |                |                 |
|------------------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                              | 1               | 0              | 2               |
| Weight decreased                               |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                              | 0               | 0              | 1               |
| White blood cell count decreased               |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                              | 0               | 1              | 0               |
| Injury, poisoning and procedural complications |                 |                |                 |
| Intentional overdose                           |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0               |
| Injection related reaction                     |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0               |
| Infusion related reaction                      |                 |                |                 |
| subjects affected / exposed                    | 8 / 15 (53.33%) | 0 / 4 (0.00%)  | 4 / 15 (26.67%) |
| occurrences (all)                              | 16              | 0              | 7               |
| Gastrointestinal anastomotic leak              |                 |                |                 |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                              | 1               | 0              | 0               |
| Facial bones fracture                          |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0               |
| Corneal abrasion                               |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                              | 0               | 0              | 1               |
| Accidental overdose                            |                 |                |                 |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                              | 0               | 0              | 1               |
| Stoma site rash                                |                 |                |                 |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                              | 1               | 0              | 0               |
| Procedural pain                                |                 |                |                 |

|                                                  |                     |                    |                     |
|--------------------------------------------------|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Cardiac disorders                                |                     |                    |                     |
| Atrial fibrillation                              |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Palpitations                                     |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Sinus tachycardia                                |                     |                    |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 1                   | 0                  | 0                   |
| Tachycardia                                      |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Nervous system disorders                         |                     |                    |                     |
| Dizziness                                        |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 3 / 15 (20.00%)     |
| occurrences (all)                                | 0                   | 0                  | 4                   |
| Cerebellar syndrome                              |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 1 / 15 (6.67%)      |
| occurrences (all)                                | 0                   | 0                  | 1                   |
| Disturbance in attention                         |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Dysgeusia                                        |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Headache                                         |                     |                    |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 1 / 4 (25.00%)     | 2 / 15 (13.33%)     |
| occurrences (all)                                | 1                   | 1                  | 2                   |
| Hyperaesthesia                                   |                     |                    |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 4 (0.00%)      | 0 / 15 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Myoclonus                                        |                     |                    |                     |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed          | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Peripheral motor neuropathy          |                |                |                 |
| subjects affected / exposed          | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0              | 0              | 2               |
| Peripheral sensory neuropathy        |                |                |                 |
| subjects affected / exposed          | 1 / 15 (6.67%) | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                    | 1              | 0              | 2               |
| Sciatica                             |                |                |                 |
| subjects affected / exposed          | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Syncope                              |                |                |                 |
| subjects affected / exposed          | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Neuropathy peripheral                |                |                |                 |
| subjects affected / exposed          | 1 / 15 (6.67%) | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                    | 1              | 0              | 2               |
| Blood and lymphatic system disorders |                |                |                 |
| Thrombocytopenia                     |                |                |                 |
| subjects affected / exposed          | 1 / 15 (6.67%) | 1 / 4 (25.00%) | 2 / 15 (13.33%) |
| occurrences (all)                    | 1              | 1              | 2               |
| Anaemia                              |                |                |                 |
| subjects affected / exposed          | 1 / 15 (6.67%) | 1 / 4 (25.00%) | 3 / 15 (20.00%) |
| occurrences (all)                    | 1              | 1              | 4               |
| Lymphopenia                          |                |                |                 |
| subjects affected / exposed          | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                    | 0              | 0              | 2               |
| Neutropenia                          |                |                |                 |
| subjects affected / exposed          | 1 / 15 (6.67%) | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 1              | 1              | 0               |
| Ear and labyrinth disorders          |                |                |                 |
| Ear haemorrhage                      |                |                |                 |
| subjects affected / exposed          | 0 / 15 (0.00%) | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Ear discomfort                       |                |                |                 |

|                                                                           |                      |                     |                      |
|---------------------------------------------------------------------------|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                          | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Eye disorders                                                             |                      |                     |                      |
| Lacrimation increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)        | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Gastrointestinal disorders                                                |                      |                     |                      |
| Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Ascites<br>subjects affected / exposed<br>occurrences (all)               | 0 / 15 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Anal haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 1 / 15 (6.67%)<br>1  | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)  | 3 / 15 (20.00%)<br>5 | 1 / 4 (25.00%)<br>1 | 0 / 15 (0.00%)<br>0  |
| Abdominal pain lower<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1  | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)        | 3 / 15 (20.00%)<br>3 | 1 / 4 (25.00%)<br>1 | 4 / 15 (26.67%)<br>4 |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 | 0 / 15 (0.00%)<br>0  |
| Colitis                                                                   |                      |                     |                      |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Dry mouth                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 1 / 4 (25.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0               | 1               | 1               |
| Diarrhoea                        |                 |                 |                 |
| subjects affected / exposed      | 6 / 15 (40.00%) | 2 / 4 (50.00%)  | 4 / 15 (26.67%) |
| occurrences (all)                | 9               | 4               | 6               |
| Constipation                     |                 |                 |                 |
| subjects affected / exposed      | 3 / 15 (20.00%) | 0 / 4 (0.00%)   | 3 / 15 (20.00%) |
| occurrences (all)                | 3               | 0               | 3               |
| Dyspepsia                        |                 |                 |                 |
| subjects affected / exposed      | 4 / 15 (26.67%) | 0 / 4 (0.00%)   | 1 / 15 (6.67%)  |
| occurrences (all)                | 4               | 0               | 1               |
| Odynophagia                      |                 |                 |                 |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Nausea                           |                 |                 |                 |
| subjects affected / exposed      | 3 / 15 (20.00%) | 4 / 4 (100.00%) | 2 / 15 (13.33%) |
| occurrences (all)                | 5               | 11              | 2               |
| Haemorrhoids                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Dysphagia                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Gastrooesophageal reflux disease |                 |                 |                 |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Frequent bowel movements         |                 |                 |                 |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Enterocolitis                    |                 |                 |                 |
| subjects affected / exposed      | 1 / 15 (6.67%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                | 1               | 0               | 0               |
| Gingival bleeding                |                 |                 |                 |

|                                        |                 |                 |                 |
|----------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed            | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Vomiting                               |                 |                 |                 |
| subjects affected / exposed            | 4 / 15 (26.67%) | 4 / 4 (100.00%) | 2 / 15 (13.33%) |
| occurrences (all)                      | 7               | 6               | 2               |
| Stomatitis                             |                 |                 |                 |
| subjects affected / exposed            | 2 / 15 (13.33%) | 0 / 4 (0.00%)   | 4 / 15 (26.67%) |
| occurrences (all)                      | 2               | 0               | 6               |
| Salivary duct inflammation             |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 1 / 4 (25.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0               | 1               | 0               |
| Rectal haemorrhage                     |                 |                 |                 |
| subjects affected / exposed            | 1 / 15 (6.67%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0               |
| Proctalgia                             |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Post-tussive vomiting                  |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Oral pain                              |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Hepatobiliary disorders                |                 |                 |                 |
| Hyperbilirubinaemia                    |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 1 / 15 (6.67%)  |
| occurrences (all)                      | 0               | 0               | 1               |
| Hepatic vein thrombosis                |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 0 / 4 (0.00%)   | 1 / 15 (6.67%)  |
| occurrences (all)                      | 0               | 0               | 1               |
| Jaundice                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 15 (0.00%)  | 1 / 4 (25.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0               | 1               | 0               |
| Skin and subcutaneous tissue disorders |                 |                 |                 |
| Dermatitis acneiform                   |                 |                 |                 |

|                                            |                 |                |                 |
|--------------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                          | 0               | 0              | 2               |
| Alopecia                                   |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                          | 0               | 0              | 2               |
| Dry skin                                   |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                          | 0               | 0              | 1               |
| Erythema                                   |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Hair colour changes                        |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Hyperhidrosis                              |                 |                |                 |
| subjects affected / exposed                | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                          | 1               | 0              | 0               |
| Rash                                       |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                          | 0               | 0              | 1               |
| Night sweats                               |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                          | 0               | 1              | 1               |
| Palmar-plantar erythrodysesthesia syndrome |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 4 / 15 (26.67%) |
| occurrences (all)                          | 0               | 0              | 6               |
| Pruritus                                   |                 |                |                 |
| subjects affected / exposed                | 2 / 15 (13.33%) | 0 / 4 (0.00%)  | 3 / 15 (20.00%) |
| occurrences (all)                          | 2               | 0              | 3               |
| Psoriasis                                  |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Hyperkeratosis                             |                 |                |                 |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |

|                                                                            |                     |                    |                      |
|----------------------------------------------------------------------------|---------------------|--------------------|----------------------|
| Rash macular<br>subjects affected / exposed<br>occurrences (all)           | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)    | 1 / 15 (6.67%)<br>1 | 0 / 4 (0.00%)<br>0 | 6 / 15 (40.00%)<br>8 |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)           | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Seborrhoeic dermatitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)              | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Xeroderma<br>subjects affected / exposed<br>occurrences (all)              | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Skin exfoliation<br>subjects affected / exposed<br>occurrences (all)       | 1 / 15 (6.67%)<br>2 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Renal and urinary disorders                                                |                     |                    |                      |
| Urinary incontinence<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)                | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)            | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 | 2 / 15 (13.33%)<br>2 |
| Renal pain                                                                 |                     |                    |                      |

|                                                                                                                   |                     |                     |                      |
|-------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Acute kidney injury<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 15 (0.00%)<br>0 | 1 / 4 (25.00%)<br>1 | 1 / 15 (6.67%)<br>1  |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1 | 1 / 4 (25.00%)<br>1 | 2 / 15 (13.33%)<br>2 |
| Arthritis<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)                                                    | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)                                                    | 1 / 15 (6.67%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Fracture pain<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 15 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Back pain                                                                                                         |                     |                     |                      |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 15 (20.00%) | 1 / 4 (25.00%) | 3 / 15 (20.00%) |
| occurrences (all)           | 3               | 1              | 3               |
| Muscle discomfort           |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Muscle spasms               |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Musculoskeletal pain        |                 |                |                 |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Myalgia                     |                 |                |                 |
| subjects affected / exposed | 2 / 15 (13.33%) | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 3               | 1              | 0               |
| Neck pain                   |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Pain in extremity           |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Infections and infestations |                 |                |                 |
| Nasopharyngitis             |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Influenza                   |                 |                |                 |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Gingivitis                  |                 |                |                 |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Otitis media                |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Sinusitis                   |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |

|                                    |                 |                |                 |
|------------------------------------|-----------------|----------------|-----------------|
| Sepsis                             |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                  | 0               | 0              | 1               |
| Rash pustular                      |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| Pneumonia                          |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| Soft tissue infection              |                 |                |                 |
| subjects affected / exposed        | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                  | 1               | 0              | 1               |
| Tooth infection                    |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0               | 1              | 0               |
| Urinary tract infection            |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| Upper respiratory tract infection  |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| Metabolism and nutrition disorders |                 |                |                 |
| Decreased appetite                 |                 |                |                 |
| subjects affected / exposed        | 5 / 15 (33.33%) | 1 / 4 (25.00%) | 5 / 15 (33.33%) |
| occurrences (all)                  | 6               | 1              | 7               |
| Dehydration                        |                 |                |                 |
| subjects affected / exposed        | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0               |
| Hyperkalaemia                      |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                  | 0               | 0              | 1               |
| Hyperphosphataemia                 |                 |                |                 |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0               |
| Hypoalbuminaemia                   |                 |                |                 |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 1               | 0              | 2               |
| Malnutrition                |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Hypokalaemia                |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Hypomagnesaemia             |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Hyponatraemia               |                 |                |                 |
| subjects affected / exposed | 3 / 15 (20.00%) | 0 / 4 (0.00%)  | 3 / 15 (20.00%) |
| occurrences (all)           | 3               | 0              | 3               |
| Hypophosphataemia           |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 4 (25.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Hypocalcaemia               |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Type 2 diabetes mellitus    |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Vitamin D deficiency        |                 |                |                 |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 4 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |

| <b>Non-serious adverse events</b>                                   | Atezolizumab +<br>Regorafenib | Atezolizumab +<br>LOAd703 |  |
|---------------------------------------------------------------------|-------------------------------|---------------------------|--|
| Total subjects affected by non-serious adverse events               |                               |                           |  |
| subjects affected / exposed                                         | 15 / 15 (100.00%)             | 2 / 2 (100.00%)           |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                               |                           |  |
| Tumour fistulisation                                                |                               |                           |  |
| subjects affected / exposed                                         | 0 / 15 (0.00%)                | 0 / 2 (0.00%)             |  |
| occurrences (all)                                                   | 0                             | 0                         |  |
| Tumour pain                                                         |                               |                           |  |

|                                                         |                     |                    |  |
|---------------------------------------------------------|---------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all)        | 1 / 15 (6.67%)<br>1 | 0 / 2 (0.00%)<br>0 |  |
| Vascular disorders                                      |                     |                    |  |
| Vena cava thrombosis                                    |                     |                    |  |
| subjects affected / exposed                             | 0 / 15 (0.00%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 0                   | 0                  |  |
| Hypertension                                            |                     |                    |  |
| subjects affected / exposed                             | 2 / 15 (13.33%)     | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 2                   | 0                  |  |
| General disorders and administration<br>site conditions |                     |                    |  |
| Asthenia                                                |                     |                    |  |
| subjects affected / exposed                             | 5 / 15 (33.33%)     | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 5                   | 0                  |  |
| Chest discomfort                                        |                     |                    |  |
| subjects affected / exposed                             | 0 / 15 (0.00%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 0                   | 0                  |  |
| Chest pain                                              |                     |                    |  |
| subjects affected / exposed                             | 2 / 15 (13.33%)     | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 2                   | 0                  |  |
| Chills                                                  |                     |                    |  |
| subjects affected / exposed                             | 0 / 15 (0.00%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 0                   | 0                  |  |
| Inflammation                                            |                     |                    |  |
| subjects affected / exposed                             | 1 / 15 (6.67%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                  |  |
| General physical health deterioration                   |                     |                    |  |
| subjects affected / exposed                             | 1 / 15 (6.67%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                  |  |
| Non-cardiac chest pain                                  |                     |                    |  |
| subjects affected / exposed                             | 0 / 15 (0.00%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 0                   | 0                  |  |
| Mucosal inflammation                                    |                     |                    |  |
| subjects affected / exposed                             | 0 / 15 (0.00%)      | 0 / 2 (0.00%)      |  |
| occurrences (all)                                       | 0                   | 0                  |  |
| Medical device site erythema                            |                     |                    |  |

|                                         |                 |                 |
|-----------------------------------------|-----------------|-----------------|
| subjects affected / exposed             | 1 / 15 (6.67%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 1               | 0               |
| Injection site reaction                 |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Influenza like illness                  |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Device related thrombosis               |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Face oedema                             |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Fatigue                                 |                 |                 |
| subjects affected / exposed             | 7 / 15 (46.67%) | 2 / 2 (100.00%) |
| occurrences (all)                       | 8               | 2               |
| Oedema                                  |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Systemic inflammatory response syndrome |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Pyrexia                                 |                 |                 |
| subjects affected / exposed             | 2 / 15 (13.33%) | 0 / 2 (0.00%)   |
| occurrences (all)                       | 3               | 0               |
| Peripheral swelling                     |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Pain                                    |                 |                 |
| subjects affected / exposed             | 0 / 15 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                       | 0               | 0               |
| Oedema peripheral                       |                 |                 |
| subjects affected / exposed             | 2 / 15 (13.33%) | 0 / 2 (0.00%)   |
| occurrences (all)                       | 2               | 0               |

|                                                                                                                            |                      |                     |  |
|----------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------|--|
| Swelling face<br>subjects affected / exposed<br>occurrences (all)                                                          | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  |  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  |  |
| Cytokine release syndrome<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 15 (0.00%)<br>0  | 1 / 2 (50.00%)<br>1 |  |
| Reproductive system and breast disorders<br>Intermenstrual bleeding<br>subjects affected / exposed<br>occurrences (all)    | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  |  |
| Perineal fistula<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  |  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                                    | 1 / 15 (6.67%)<br>1  | 0 / 2 (0.00%)<br>0  |  |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  | 0 / 2 (0.00%)<br>0  |  |
| Aspiration<br>subjects affected / exposed<br>occurrences (all)                                                             | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                                                  | 2 / 15 (13.33%)<br>2 | 0 / 2 (0.00%)<br>0  |  |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                                                              | 3 / 15 (20.00%)<br>3 | 0 / 2 (0.00%)<br>0  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                               | 3 / 15 (20.00%)<br>3 | 1 / 2 (50.00%)<br>2 |  |

|                             |                |               |  |
|-----------------------------|----------------|---------------|--|
| Aphonia                     |                |               |  |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 1              | 0             |  |
| Epistaxis                   |                |               |  |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 1              | 0             |  |
| Haemoptysis                 |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypoxia                     |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Nasal congestion            |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Nasal dryness               |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Rhinorrhoea                 |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Sinus congestion            |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Wheezing                    |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Oropharyngeal pain          |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Psychiatric disorders       |                |               |  |
| Agitation                   |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Anxiety                     |                |               |  |

|                                                                                                 |                      |                    |  |
|-------------------------------------------------------------------------------------------------|----------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 15 (6.67%)<br>1  | 0 / 2 (0.00%)<br>0 |  |
| Product issues<br>Device occlusion<br>subjects affected / exposed<br>occurrences (all)          | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Investigations<br>Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>2  | 0 / 2 (0.00%)<br>0 |  |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)        | 3 / 15 (20.00%)<br>3 | 0 / 2 (0.00%)<br>0 |  |
| Alanine aminotransferase increased                                                              |                      |                    |  |

|                                                |                 |               |  |
|------------------------------------------------|-----------------|---------------|--|
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Blood alkaline phosphatase increased           |                 |               |  |
| subjects affected / exposed                    | 2 / 15 (13.33%) | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 2               | 0             |  |
| Electrocardiogram QT prolonged                 |                 |               |  |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Gamma-glutamyltransferase increased            |                 |               |  |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Lipase increased                               |                 |               |  |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Lymphocyte count decreased                     |                 |               |  |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Lymphocyte count increased                     |                 |               |  |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Neutrophil count decreased                     |                 |               |  |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 1               | 0             |  |
| Platelet count decreased                       |                 |               |  |
| subjects affected / exposed                    | 3 / 15 (20.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 4               | 0             |  |
| Weight decreased                               |                 |               |  |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 1               | 0             |  |
| White blood cell count decreased               |                 |               |  |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Injury, poisoning and procedural complications |                 |               |  |

|                                                                                       |                      |                    |  |
|---------------------------------------------------------------------------------------|----------------------|--------------------|--|
| Intentional overdose<br>subjects affected / exposed<br>occurrences (all)              | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Injection related reaction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Infusion related reaction<br>subjects affected / exposed<br>occurrences (all)         | 2 / 15 (13.33%)<br>2 | 0 / 2 (0.00%)<br>0 |  |
| Gastrointestinal anastomotic leak<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Facial bones fracture<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Corneal abrasion<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Accidental overdose<br>subjects affected / exposed<br>occurrences (all)               | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Stoma site rash<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Cardiac disorders                                                                     |                      |                    |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)               | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Sinus tachycardia                                                                     |                      |                    |  |

|                               |                |               |  |
|-------------------------------|----------------|---------------|--|
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Tachycardia                   |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Nervous system disorders      |                |               |  |
| Dizziness                     |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Cerebellar syndrome           |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Disturbance in attention      |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Dysgeusia                     |                |               |  |
| subjects affected / exposed   | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 1              | 0             |  |
| Headache                      |                |               |  |
| subjects affected / exposed   | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 1              | 0             |  |
| Hyperaesthesia                |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Myoclonus                     |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Peripheral motor neuropathy   |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Peripheral sensory neuropathy |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |
| Sciatica                      |                |               |  |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)             | 0              | 0             |  |

|                                                                           |                      |                    |  |
|---------------------------------------------------------------------------|----------------------|--------------------|--|
| Syncope<br>subjects affected / exposed<br>occurrences (all)               | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Neuropathy peripheral<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Blood and lymphatic system disorders                                      |                      |                    |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)      | 2 / 15 (13.33%)<br>2 | 0 / 2 (0.00%)<br>0 |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)               | 3 / 15 (20.00%)<br>3 | 0 / 2 (0.00%)<br>0 |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 15 (6.67%)<br>1  | 0 / 2 (0.00%)<br>0 |  |
| Ear and labyrinth disorders                                               |                      |                    |  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)       | 1 / 15 (6.67%)<br>1  | 0 / 2 (0.00%)<br>0 |  |
| Ear discomfort<br>subjects affected / exposed<br>occurrences (all)        | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Eye disorders                                                             |                      |                    |  |
| Lacrimation increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)        | 0 / 15 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 |  |
| Gastrointestinal disorders                                                |                      |                    |  |

|                             |                 |                |
|-----------------------------|-----------------|----------------|
| Abdominal discomfort        |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Ascites                     |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Anal haemorrhage            |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Abdominal pain upper        |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Abdominal pain lower        |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Abdominal pain              |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 1 / 2 (50.00%) |
| occurrences (all)           | 2               | 1              |
| Abdominal distension        |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 1 / 2 (50.00%) |
| occurrences (all)           | 1               | 1              |
| Colitis                     |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Dry mouth                   |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0               | 0              |
| Diarrhoea                   |                 |                |
| subjects affected / exposed | 7 / 15 (46.67%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 8               | 0              |
| Constipation                |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 1               | 0              |
| Dyspepsia                   |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 1               | 0              |

|                                  |                 |                |
|----------------------------------|-----------------|----------------|
| Odynophagia                      |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Nausea                           |                 |                |
| subjects affected / exposed      | 3 / 15 (20.00%) | 1 / 2 (50.00%) |
| occurrences (all)                | 3               | 1              |
| Haemorrhoids                     |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Dysphagia                        |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Gastrooesophageal reflux disease |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Frequent bowel movements         |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Enterocolitis                    |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Gingival bleeding                |                 |                |
| subjects affected / exposed      | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 1               | 0              |
| Vomiting                         |                 |                |
| subjects affected / exposed      | 3 / 15 (20.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                | 4               | 0              |
| Stomatitis                       |                 |                |
| subjects affected / exposed      | 3 / 15 (20.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                | 3               | 0              |
| Salivary duct inflammation       |                 |                |
| subjects affected / exposed      | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Rectal haemorrhage               |                 |                |
| subjects affected / exposed      | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 1               | 0              |

|                                        |                |               |  |
|----------------------------------------|----------------|---------------|--|
| Proctalgia                             |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Post-tussive vomiting                  |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Oral pain                              |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Hepatobiliary disorders                |                |               |  |
| Hyperbilirubinaemia                    |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Hepatic vein thrombosis                |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Jaundice                               |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Skin and subcutaneous tissue disorders |                |               |  |
| Dermatitis acneiform                   |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Alopecia                               |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Dry skin                               |                |               |  |
| subjects affected / exposed            | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 1              | 0             |  |
| Erythema                               |                |               |  |
| subjects affected / exposed            | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 1              | 0             |  |
| Hair colour changes                    |                |               |  |
| subjects affected / exposed            | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Hyperhidrosis                          |                |               |  |

|                                            |                 |                |
|--------------------------------------------|-----------------|----------------|
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 0               | 0              |
| Rash                                       |                 |                |
| subjects affected / exposed                | 2 / 15 (13.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                          | 2               | 0              |
| Night sweats                               |                 |                |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 0               | 0              |
| Palmar-plantar erythrodysesthesia syndrome |                 |                |
| subjects affected / exposed                | 5 / 15 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                          | 7               | 0              |
| Pruritus                                   |                 |                |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 0               | 0              |
| Psoriasis                                  |                 |                |
| subjects affected / exposed                | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 1               | 0              |
| Hyperkeratosis                             |                 |                |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 0               | 0              |
| Rash macular                               |                 |                |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 0               | 0              |
| Rash maculo-papular                        |                 |                |
| subjects affected / exposed                | 3 / 15 (20.00%) | 1 / 2 (50.00%) |
| occurrences (all)                          | 4               | 1              |
| Rash papular                               |                 |                |
| subjects affected / exposed                | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 1               | 0              |
| Seborrhoeic dermatitis                     |                 |                |
| subjects affected / exposed                | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 0               | 0              |
| Urticaria                                  |                 |                |
| subjects affected / exposed                | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |
| occurrences (all)                          | 1               | 0              |

|                                                                                                         |                     |                    |  |
|---------------------------------------------------------------------------------------------------------|---------------------|--------------------|--|
| Xeroderma<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 15 (6.67%)<br>1 | 0 / 2 (0.00%)<br>0 |  |
| Skin exfoliation<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Renal and urinary disorders<br>Urinary incontinence<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)                                             | 1 / 15 (6.67%)<br>1 | 0 / 2 (0.00%)<br>0 |  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)                                         | 1 / 15 (6.67%)<br>1 | 0 / 2 (0.00%)<br>0 |  |
| Renal pain<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 15 (6.67%)<br>1 | 0 / 2 (0.00%)<br>0 |  |
| Acute kidney injury<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)               | 1 / 15 (6.67%)<br>1 | 0 / 2 (0.00%)<br>0 |  |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Musculoskeletal and connective tissue disorders                                                         |                     |                    |  |

|                             |                 |               |
|-----------------------------|-----------------|---------------|
| Arthralgia                  |                 |               |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 2 (0.00%) |
| occurrences (all)           | 3               | 0             |
| Arthritis                   |                 |               |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 1               | 0             |
| Groin pain                  |                 |               |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0               | 0             |
| Bone pain                   |                 |               |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0               | 0             |
| Flank pain                  |                 |               |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0               | 0             |
| Fracture pain               |                 |               |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0               | 0             |
| Back pain                   |                 |               |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 1               | 0             |
| Muscle discomfort           |                 |               |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0               | 0             |
| Muscle spasms               |                 |               |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0               | 0             |
| Musculoskeletal pain        |                 |               |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 1               | 0             |
| Myalgia                     |                 |               |
| subjects affected / exposed | 4 / 15 (26.67%) | 0 / 2 (0.00%) |
| occurrences (all)           | 4               | 0             |
| Neck pain                   |                 |               |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 1               | 0             |

|                                                                           |                     |                    |  |
|---------------------------------------------------------------------------|---------------------|--------------------|--|
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)     | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Infections and infestations                                               |                     |                    |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Gingivitis<br>subjects affected / exposed<br>occurrences (all)            | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Otitis media<br>subjects affected / exposed<br>occurrences (all)          | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Sepsis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Rash pustular<br>subjects affected / exposed<br>occurrences (all)         | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Soft tissue infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 15 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |  |
| Urinary tract infection                                                   |                     |                    |  |

|                                    |                 |                |  |
|------------------------------------|-----------------|----------------|--|
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 0               | 0              |  |
| Upper respiratory tract infection  |                 |                |  |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 0               | 0              |  |
| Metabolism and nutrition disorders |                 |                |  |
| Decreased appetite                 |                 |                |  |
| subjects affected / exposed        | 6 / 15 (40.00%) | 1 / 2 (50.00%) |  |
| occurrences (all)                  | 6               | 1              |  |
| Dehydration                        |                 |                |  |
| subjects affected / exposed        | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 1               | 0              |  |
| Hyperkalaemia                      |                 |                |  |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 0               | 0              |  |
| Hyperphosphataemia                 |                 |                |  |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 0               | 0              |  |
| Hypoalbuminaemia                   |                 |                |  |
| subjects affected / exposed        | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 1               | 0              |  |
| Malnutrition                       |                 |                |  |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 0               | 0              |  |
| Hypokalaemia                       |                 |                |  |
| subjects affected / exposed        | 2 / 15 (13.33%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 2               | 0              |  |
| Hypomagnesaemia                    |                 |                |  |
| subjects affected / exposed        | 0 / 15 (0.00%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 0               | 0              |  |
| Hyponatraemia                      |                 |                |  |
| subjects affected / exposed        | 1 / 15 (6.67%)  | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 1               | 0              |  |
| Hypophosphataemia                  |                 |                |  |
| subjects affected / exposed        | 2 / 15 (13.33%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                  | 2               | 0              |  |

|                             |                |               |  |
|-----------------------------|----------------|---------------|--|
| Hypocalcaemia               |                |               |  |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 1              | 0             |  |
| Type 2 diabetes mellitus    |                |               |  |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 1              | 0             |  |
| Vitamin D deficiency        |                |               |  |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 16 October 2018  | Amended to allow enrollment into one new experimental arm for the existing cohort of patients who progressed during or following two separate lines of treatment for metastatic colorectal cancer (mCRC). The new arm is Atezolizumab + Selicrelumab + Bevacizumab.                                                                                                                              |
| 10 July 2019     | Amended primarily to reflect the addition of an experimental arm Atezolizumab + Idasanutlin in Stage 1, to clarify discrepancies and errors identified in Version 2 of the protocol, and to align the adverse event management guidelines with the recent updates to the Atezolizumab Investigator Brochure (Version 13).                                                                        |
| 29 October 2019  | Protocol CO39612 has been amended primarily to reflect the changes requested by French National Agency for the Safety of Medicines and Health Products (ANSM) in relation to the substantial amendment for protocol version 3 dated 10th July 2019.                                                                                                                                              |
| 12 November 2019 | Amended primarily to reflect the addition of two new experimental arms Atezolizumab + Regorafenib, and Atezolizumab + Regorafenib + AB928 in Stage 1, to clarify discrepancies and errors identified in Version 3 of the protocol, and to align the adverse event management guidelines with recent updates to the Atezolizumab Investigator's Brochure (Version 14).                            |
| 10 January 2020  | Amended primarily to reflect the changes requested by French National Agency for the Safety of Medicines and Health Products (ANSM) in relation to the substantial amendment for protocol Version 3 (10 July 2019) that was implemented in Version 4 (France) and to align the adverse event management guidelines with recent updates to the Atezolizumab Investigator's Brochure (Version 15). |
| 22 March 2020    | Version 7, is a merging of the global protocol (previously Version 5) and the country-specific Version 6 (France, Switzerland, and United Kingdom). This amendment includes cumulative changes to the protocol from Version 5 along with global changes specific to this amendment.                                                                                                              |
| 16 January 2021  | Amended primarily to reflect the addition of a new experimental arm in Stage 1: Atezolizumab + Lokon oncolytic adenovirus (LOAd703).                                                                                                                                                                                                                                                             |
| 16 February 2021 | Amended primarily to update the eligibility criteria in Stage 1 of the Atezolizumab + Lokon oncolytic adenovirus (LOAd703) arm.                                                                                                                                                                                                                                                                  |
| 30 August 2021   | Amended to update contraception duration following a request by the U.K. Medicines and Healthcare products Regulatory Agency (MHRA).                                                                                                                                                                                                                                                             |
| 22 March 2022    | Amended primarily to reflect the removal of Imprime PGG arm, alignment with Morpheus Platform Template (including removal of iRECIST language), and alignment with Atezolizumab IB v18, and Atezolizumab model document.                                                                                                                                                                         |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study is not designed to make explicit power and Type I error considerations for a hypothesis test. Instead, this study is designed to obtain preliminary data. Due to the limited sample size, the results need to be interpreted with caution.

Notes: