



## Clinical trial results:

### A Phase 2, Multicenter, Open-Label Study of INCB050465, a PI3K Inhibitor, in Relapsed or Refractory Follicular Lymphoma

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2017-001624-22          |
| Trial protocol           | GB CZ DK SE DE HU ES IT |
| Global end of trial date | 07 June 2024            |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 29 March 2025  |
| First version publication date | 26 February 2025   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Revisions made to align with updated ClinicalTrials.gov summary. |

#### Trial information

##### Trial identification

|                       |                              |
|-----------------------|------------------------------|
| Sponsor protocol code | INCB 50465-203 (CITADEL-203) |
|-----------------------|------------------------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Incyte Corporation   |
| Sponsor organisation address | 1801 Augustine Cutoff Drive, Wilmington, United States, 19803        |
| Public contact               | Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com |
| Scientific contact           | Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.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                       | 07 June 2024 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 07 June 2024 |
| Was the trial ended prematurely? | No           |

Notes:

## General information about the trial

Main objective of the trial:

This study was conducted to assess the efficacy of INCB050465 in terms of objective response rate (ORR) in participants with relapsed or refractory follicular lymphoma (FL).

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, Good Clinical Practices as defined in Title 21 of the United States Code of Federal Regulations Parts 11, 50, 54, 56, and 312, as well as International Council on Harmonisation Good Clinical Practice consolidated guidelines (E6) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 14 March 2018 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Canada: 1          |
| Country: Number of subjects enrolled | Czechia: 17        |
| Country: Number of subjects enrolled | Germany: 3         |
| Country: Number of subjects enrolled | Denmark: 3         |
| Country: Number of subjects enrolled | Spain: 18          |
| Country: Number of subjects enrolled | United Kingdom: 17 |
| Country: Number of subjects enrolled | Hungary: 4         |
| Country: Number of subjects enrolled | Israel: 10         |
| Country: Number of subjects enrolled | Italy: 15          |
| Country: Number of subjects enrolled | Poland: 3          |
| Country: Number of subjects enrolled | Sweden: 6          |
| Country: Number of subjects enrolled | United States: 29  |
| Worldwide total number of subjects   | 126                |
| EEA total number of subjects         | 69                 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                      | 50 |
| From 65 to 84 years                       | 72 |
| 85 years and over                         | 4  |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 44 investigative sites in the United States, Italy, Spain, Great Britain, Czech Republic, Hungary, Canada, Denmark, Germany, Israel, Poland, and Sweden

### Pre-assignment

Screening details:

A total of 126 participants with relapsed or refractory follicular lymphoma were enrolled in the study and assigned to one of two treatment groups: Treatment A or Treatment B to receive parsaclisib.

### Period 1

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

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW |

Arm description:

Participants received parsaclisib 20 milligrams (mg) once daily (QD) for 8 weeks followed by 20 mg once weekly (QW) for up to approximately 52 weeks.

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

Dosage and administration details:

1 mg, 2.5 mg, 5 mg, and 20 mg tablets taken orally

|                  |  |
|------------------|--|
| <b>Arm title</b> | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |
|------------------|--|

Arm description:

Participants received parsaclisib 20 mg QD for 8 weeks followed by 2.5 mg QD for up to approximately 52 weeks.

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

Dosage and administration details:

1 mg, 2.5 mg, 5 mg, and 20 mg tablets taken orally

| <b>Number of subjects in period 1</b> | Parsaclisib 20 mg<br>QD for 8 Weeks<br>followed by 20 mg<br>QW | Parsaclisib 20 mg<br>QD for 8 Weeks<br>followed by 2.5 mg<br>QD |
|---------------------------------------|--|---|
| Started                               | 23   | 103   |
| Completed                             | 14   | 50  |
| Not completed                         | 9  | 53  |
| Consent withdrawn by subject          | 1  | 9   |
| Physician decision                    | 1  | -   |
| Site Closed                           | -  | 1   |
| Death                                 | 5  | 27  |
| Did Not Return to Site for Care       | -  | 1   |
| Lost to follow-up                     | 2  | 4   |
| Transitioned to Rollover Study        | -  | 11  |

## Baseline characteristics

### Reporting groups

|   |  |
|---|--|
| Reporting group title   | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW  |
| Reporting group description:  |  |
| Participants received parsaclisib 20 milligrams (mg) once daily (QD) for 8 weeks followed by 20 mg once weekly (QW) for up to approximately 52 weeks. |  |
| Reporting group title   | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |
| Reporting group description:  |  |
| Participants received parsaclisib 20 mg QD for 8 weeks followed by 2.5 mg QD for up to approximately 52 weeks.  |  |

| Reporting group values                             | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD | Total |
|--|---|--|-------|
| Number of subjects                                 | 23  | 103  | 126   |
| Age categorical<br>Units: Subjects                 |   |  |       |
| In utero   | 0   | 0  | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 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     |
| Adolescents (12-17 years)                          | 0   | 0  | 0     |
| Adults (18-64 years)                               | 11  | 39   | 50    |
| From 65-84 years                                   | 12  | 60   | 72    |
| 85 years and over                                  | 0   | 4  | 4     |
| Age Continuous<br>Units: years                     |   |  |       |
| arithmetic mean                                    | 64.1  | 67.0   | -     |
| standard deviation                                 | ± 11.56   | ± 10.68  | -     |
| Sex: Female, Male<br>Units: participants           |   |  |       |
| Female   | 11  | 45   | 56    |
| Male   | 12  | 58   | 70    |
| Ethnicity (NIH/OMB)<br>Units: Subjects             |   |  |       |
| Hispanic or Latino                                 | 1   | 6  | 7     |
| Not Hispanic or Latino                             | 19  | 90   | 109   |
| Unknown or Not Reported                            | 3   | 7  | 10    |
| Race Customized<br>Units: Subjects                 |   |  |       |
| Asian  | 0   | 1  | 1     |
| Black/ African- American                           | 1   | 6  | 7     |
| White/ Caucasian                                   | 21  | 92   | 113   |
| Unavailable or Unknown                             | 1   | 4  | 5     |

## End points

### End points reporting groups

|   |  |
|---|--|
| Reporting group title   | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW  |
| Reporting group description:<br>Participants received parsaclisib 20 milligrams (mg) once daily (QD) for 8 weeks followed by 20 mg once weekly (QW) for up to approximately 52 weeks. |  |
| Reporting group title   | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |
| Reporting group description:<br>Participants received parsaclisib 20 mg QD for 8 weeks followed by 2.5 mg QD for up to approximately 52 weeks.  |  |

### Primary: Objective Response Rate With Parsaclisib Based on Lugano Classification Response Criteria

|   |  |
|---|--|
| End point title   | Objective Response Rate With Parsaclisib Based on Lugano Classification Response Criteria <sup>[1]</sup> |
| End point description:<br>ORR=percentage of participants with complete response(CR) or partial response(PR) per revised response criteria for lymphomas,determined by independent review committee(IRC).Criteria for CR:1.Target nodes/nodal masses of lymph nodes,extralymphatic sites regressed to≤1.5cm in longest dimension transverse diameter of lesion(LDi);2.Absence of non-measured lesion;3.Organ enlargement regressed to normal;4.No new lesions;5.Normal bone marrow morphology;if indeterminate,immunohistochemistry negative.Criteria for PR:1.Lymph nodes,extralymphatic sites- ≥50%decrease in sum of product of perpendicular diameters for multiple lesions( SPD)of up to 6 target measurable nodes,extranodal sites;if lesion is too small to measure on computed tomography(CT),assign5mm×5mm as default;if no longer visible,0×0mm.Node>5mm×5mm but smaller than normal,use actual measurement.2.Absent/regressed non-measured lesions,no increase.3.Organ enlargement-Spleen regressed by>50%in length beyond normal.4.No new lesions. |  |
| End point type  | Primary  |
| End point timeframe:<br>Up to approximately 148 weeks   |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not conducted for this endpoint.

| End point values                  | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed       | 23 <sup>[2]</sup>                                     | 103 <sup>[3]</sup>                                     |  |  |
| Units: percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 65.2 (42.7 to 83.6)                                   | 77.7 (68.4 to 85.3)                                    |  |  |

Notes:

[2] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[3] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

### Statistical analyses

No statistical analyses for this end point

### Secondary: Complete Response Rate With Parsaclisib Based on Lugano Classification

## Response Criteria

|                 |  |
|-----------------|--|
| End point title | Complete Response Rate With Parsaclisib Based on Lugano Classification Response Criteria |
|-----------------|--|

End point description:

CRR was defined as the percentage of participants with a CR as defined by revised response criteria for lymphomas as determined by an IRC. The criteria for CR included: 1. Target nodes/nodal masses of lymph nodes and extralymphatic sites must regress to  $\leq 1.5$  cm in LDi; 2. Absence of non-measured lesion; 3. Organ enlargement regressed to normal; 4. No new lesions; 5. Bone marrow must be normal by morphology; if indeterminate, immunohistochemistry negative.

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

End point timeframe:

Up to 1193 days

| End point values                  | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed       | 23 <sup>[4]</sup>                                     | 103 <sup>[5]</sup>                                     |  |  |
| Units: percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 17.4 (5.0 to 38.8)                                    | 22.3 (14.7 to 31.6)                                    |  |  |

Notes:

[4] - Full Analysis Set: all participants enrolled in the study who received  $\geq 1$  dose of parsaclisib

[5] - Full Analysis Set: all participants enrolled in the study who received  $\geq 1$  dose of parsaclisib

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR)

|                 |                            |
|-----------------|----------------------------|
| End point title | Duration of Response (DOR) |
|-----------------|----------------------------|

End point description:

DOR=time from first documented CR or PR until disease progression/death from any cause among participants who achieve an objective response as determined by IRC. CR: 1.Target nodes/nodal masses of lymph nodes and extralymphatic sites must regress to  $\leq 1.5$  cm in LDi; 2. Absence of non-measured lesion; 3.Organ enlargement regressed to normal; 4.No new lesions; 5.Bone marrow normal by morphology; if indeterminate, immunohistochemistry negative. PR: 1.Lymph nodes/extralymphatic sites- a.  $\geq 50\%$  decrease in SPD of up to 6 target measurable nodes/extranodal sites; b. when a lesion is too small to measure on CT, assign 5 mm $\times$ 5 mm as the default; c.when no longer visible, 0 $\times$ 0 mm. For a node  $>5$  mm $\times$ 5 mm but smaller than normal, use actual measurement. 2.Non-measured lesions- Absent/regressed, but no increase. 3. Organ enlargement-Spleen regressed by  $>50\%$  in length beyond normal. 4.No new lesions. 9999=The upper limit of the CI was not estimable due to the low number of participants with events.

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

End point timeframe:

Up to 1193 days



| End point values                 | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed      | 15 <sup>[6]</sup>                                     | 81 <sup>[7]</sup>                                      |  |  |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 14.06 (3.19 to 9999)                                  | 14.72 (11.76 to 25.72)                                 |  |  |

Notes:

[6] - Only participants with an objective response were analyzed.

[7] - Only participants with an objective response were analyzed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression-free Survival (PFS) With Parsaclisib

|  |  |
|--|--|
| End point title  | Progression-free Survival (PFS) With Parsaclisib |
| End point description:   |  |
| PFS was defined as the time from the date of the first dose of study treatment until the earliest date of disease progression, as determined by radiographic disease assessment provided by an IRC, or death from any cause. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Up to 1193 days  |  |

| End point values                 | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed      | 23 <sup>[8]</sup>                                     | 103 <sup>[9]</sup>                                     |  |  |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 19.32 (8.31 to 33.15)                                 | 14.03 (11.07 to 20.07)                                 |  |  |

Notes:

[8] - Full Analysis Set: all participants enrolled in the study who received  $\geq 1$  dose of parsaclisib

[9] - Full Analysis Set: all participants enrolled in the study who received  $\geq 1$  dose of parsaclisib

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival (OS) With Parsaclisib

|   |  |
|---|--|
| End point title   | Overall Survival (OS) With Parsaclisib |
| End point description:  |  |
| OS was defined as the time from the date of the first dose of study treatment until death from any cause. -9999, 9999=The median and the lower and upper limits of the 95% CI were not estimable due to the low number of participants with events. |  |
| End point type  | Secondary                              |
| End point timeframe:  |  |
| Up to 1193 days   |  |

| End point values                 | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed      | 23 <sup>[10]</sup>                                    | 103 <sup>[11]</sup>                                    |  |  |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 9999 (35.48 to 9999)                                  | 9999 (-9999 to 9999)                                   |  |  |

Notes:

[10] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[11] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

### Statistical analyses

No statistical analyses for this end point

### Secondary: Best Percent Change From Baseline in Target Lesion Size

|  |   |
|--|---|
| End point title  | Best Percent Change From Baseline in Target Lesion Size |
| End point description:   |   |
| Target lesion size is measured by the sum of the product of diameters of all target lesion sizes and is determined by the IRC. The best percent change from Baseline is defined as the largest decrease, or smallest increase (if no decrease available), from Baseline in target lesion sizes on/before new (next-line) anti-lymphoma therapy during the study. Baseline is the last non-missing measurement obtained before the first administration of study drug. A negative percent change from Baseline indicates improvement. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Up to 1193 days  |   |

| End point values                     | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed          | 20 <sup>[12]</sup>                                    | 98 <sup>[13]</sup>                                     |  |  |
| Units: percent change in lesion size |   |  |  |  |
| arithmetic mean (standard deviation) | -72.90 (± 21.782)                                     | -72.77 (± 31.972)                                      |  |  |

Notes:

[12] - Full Analysis Set. Only participants with available data were analyzed.

[13] - Full Analysis Set. Only participants with available data were analyzed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

|  |   |
|--|---|
| End point title  | Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) |
| End point description:   |   |
| An adverse event (AE) is defined as any untoward medical occurrence associated with use of a drug in humans, whether or not considered drug related, that occurs after a participant provides informed consent. TEAE is any AE either reported for first time or worsening of a pre-existing event after first dose of study drug and within 30 days of last administration of study drug regardless of starting new anti-lymphoma therapy. SAE is any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, leads to a congenital anomaly/birth defect or is considered to be an important medical event that may not result in death, be immediately life-threatening, or require hospitalization but may be considered serious when, based on appropriate medical judgment, the event may jeopardize the participant or may require medical or surgical intervention. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| up to approximately 1992 days  |   |

| End point values                  | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed       | 23 <sup>[14]</sup>                                    | 103 <sup>[15]</sup>                                    |  |  |
| Units: percentage of participants |   |  |  |  |
| number (not applicable)           |   |  |  |  |
| TEAEs                             | 100.0   | 99.0   |  |  |
| SAEs                              | 52.2  | 53.4   |  |  |

Notes:

[14] - Safety Population: all participants enrolled in the study who received  $\geq 1$  dose of parsaclisib

[15] - Safety Population: all participants enrolled in the study who received  $\geq 1$  dose of parsaclisib

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

up to approximately 1992 days

Adverse event reporting additional description:

Adverse events have been reported for members of the Safety Population, comprised of all participants enrolled in the study who received at least 1 dose of parsaclisib.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD |
|-----------------------|--|

Reporting group description:

Participants received parsaclisib 20 mg QD for 8 weeks followed by 2.5 mg QD for up to approximately 52 weeks.

|                       |   |
|-----------------------|---|
| Reporting group title | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW |
|-----------------------|---|

Reporting group description:

Participants received parsaclisib 20 milligrams (mg) once daily (QD) for 8 weeks followed by 20 mg once weekly (QW) for up to approximately 52 weeks.

| <b>Serious adverse events</b>                                       | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW |  |
|---|--|---|--|
| Total subjects affected by serious adverse events                   |  |   |  |
| subjects affected / exposed   | 55 / 103 (53.40%)                                      | 12 / 23 (52.17%)                                      |  |
| number of deaths (all causes)                                       | 27   | 5   |  |
| number of deaths resulting from adverse events                      | 4  | 0   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |  |
| Bladder neoplasm  |  |   |  |
| subjects affected / exposed   | 1 / 103 (0.97%)  | 0 / 23 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1  | 0 / 0   |  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   |  |
| Desmoplastic mesothelioma   |  |   |  |
| subjects affected / exposed   | 1 / 103 (0.97%)  | 0 / 23 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1  | 0 / 0   |  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   |  |
| Hepatocellular carcinoma  |  |   |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Lung neoplasm malignant                              |                 |                |  |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Vascular disorders                                   |                 |                |  |
| Deep vein thrombosis                                 |                 |                |  |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Haemorrhage  |                 |                |  |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Hypertension   |                 |                |  |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Hypotension  |                 |                |  |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| General disorders and administration site conditions |                 |                |  |
| Chest pain   |                 |                |  |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Disease progression                                  |                 |                |  |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| General physical health deterioration           |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Mucosal inflammation                            |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Non-cardiac chest pain                          |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pyrexia   |                 |                |  |
| subjects affected / exposed                     | 3 / 103 (2.91%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                 |                |  |
| Chronic obstructive pulmonary disease           |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dyspnoea  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pleural effusion                                |                 |                |  |
| subjects affected / exposed                     | 3 / 103 (2.91%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 6           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonitis                                     |                 |                |  |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Pneumothorax                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Investigations                                  |                 |                |  |
| C-reactive protein increased                    |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Body temperature increased                      |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Electrocardiogram QT prolonged                  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Neutrophil count decreased                      |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                 |                |  |
| Cervical vertebral fracture                     |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Fall  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Femoral neck fracture                           |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Hip fracture                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Overdose  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Stomal hernia                                   |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Wrist fracture                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cardiac disorders                               |                 |                |  |
| Atrial fibrillation                             |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pericardial effusion                            |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Supraventricular tachycardia                    |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sinus bradycardia                               |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Nervous system disorders                        |                 |                |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| Cerebrovascular accident                        |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cervical radiculopathy                          |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dizziness                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Encephalopathy                                  |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Headache  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Nervous system disorder                         |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lethargy  |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders            |                 |                |  |
| Anaemia   |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Febrile neutropenia                             |                 |                |  |

|   |                  |                |  |
|---|------------------|----------------|--|
| subjects affected / exposed                     | 2 / 103 (1.94%)  | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Leukocytosis                                    |                  |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%)  | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Ear and labyrinth disorders                     |                  |                |  |
| Vertigo   |                  |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%)  | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Gastrointestinal disorders                      |                  |                |  |
| Abdominal pain                                  |                  |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%)  | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Colitis erosive                                 |                  |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%)  | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Colitis   |                  |                |  |
| subjects affected / exposed                     | 8 / 103 (7.77%)  | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 8 / 8            | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Diarrhoea                                       |                  |                |  |
| subjects affected / exposed                     | 10 / 103 (9.71%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 9 / 11           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Diverticular perforation                        |                  |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%)  | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          |  |
| Immune-mediated enterocolitis                   |                  |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Intestinal pseudo-obstruction                   |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Parotid gland enlargement                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Oesophagitis                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Stomatitis                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Small intestinal obstruction                    |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Vomiting  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Skin and subcutaneous tissue disorders          |                 |                |  |
| Dermatitis exfoliative generalised              |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Stevens-Johnson syndrome                        |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| Rash  |                 |                |  |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Renal and urinary disorders                     |                 |                |  |
| Acute kidney injury                             |                 |                |  |
| subjects affected / exposed                     | 3 / 103 (2.91%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urinary tract obstruction                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Arthritis                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Arthralgia                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Back pain                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Autoimmune arthritis                            |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Musculoskeletal chest pain                      |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Neck pain                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| COVID-19  |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Campylobacter colitis                           |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bursitis infective                              |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bacteraemia                                     |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Coronavirus infection                           |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cytomegalovirus colitis                         |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastrointestinal infection                      |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastroenteritis                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Herpes zoster                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Influenza                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lower respiratory tract infection               |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lower respiratory tract infection viral         |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Oesophageal candidiasis                         |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Oral candidiasis                                |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumocystis jirovecii pneumonia                |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Subcutaneous abscess                            |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia                                       |                 |                |  |
| subjects affected / exposed                     | 3 / 103 (2.91%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 4           | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| Pneumonia mycoplasmal                           |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory tract infection                     |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urinary tract infection                         |                 |                |  |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urosepsis                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Metabolism and nutrition disorders              |                 |                |  |
| Dehydration                                     |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 2 / 23 (8.70%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypercalcaemia                                  |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hyperglycaemia                                  |                 |                |  |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hyperkalaemia                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 23 (4.35%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypokalaemia                                    |                 |                |  |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypomagnesaemia                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Metabolic acidosis                              |                 |                |  |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 23 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 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>                                   | Parsaclisib 20 mg QD for 8 Weeks followed by 2.5 mg QD | Parsaclisib 20 mg QD for 8 Weeks followed by 20 mg QW |  |
|---|--|---|--|
| Total subjects affected by non-serious adverse events               |  |   |  |
| subjects affected / exposed   | 94 / 103 (91.26%)                                      | 22 / 23 (95.65%)                                      |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |  |
| Infected neoplasm   |  |   |  |



|   |   |  |  |
|---|---|--|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 103 (0.00%)<br>0  | 2 / 23 (8.70%)<br>2  |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)  | 12 / 103 (11.65%)<br>13   | 0 / 23 (0.00%)<br>0  |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Asthenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)<br><br>Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 21 / 103 (20.39%)<br>23<br><br>14 / 103 (13.59%)<br>17<br><br>10 / 103 (9.71%)<br>10<br><br>2 / 103 (1.94%)<br>2<br><br>20 / 103 (19.42%)<br>26 | 3 / 23 (13.04%)<br>3<br><br>2 / 23 (8.70%)<br>2<br><br>1 / 23 (4.35%)<br>1<br><br>2 / 23 (8.70%)<br>2<br><br>2 / 23 (8.70%)<br>2 |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Wheezing<br>subjects affected / exposed<br>occurrences (all)   | 28 / 103 (27.18%)<br>30<br><br>8 / 103 (7.77%)<br>10<br><br>5 / 103 (4.85%)<br>7<br><br>0 / 103 (0.00%)<br>0                                    | 3 / 23 (13.04%)<br>3<br><br>0 / 23 (0.00%)<br>0<br><br>2 / 23 (8.70%)<br>2<br><br>2 / 23 (8.70%)<br>2                            |  |
| Psychiatric disorders   |   |  |  |

|  |                         |                     |  |
|--|-------------------------|---------------------|--|
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                             | 6 / 103 (5.83%)<br>6    | 0 / 23 (0.00%)<br>0 |  |
| Investigations   |                         |                     |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 7 / 103 (6.80%)<br>11   | 1 / 23 (4.35%)<br>1 |  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)         | 2 / 103 (1.94%)<br>2    | 2 / 23 (8.70%)<br>2 |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 8 / 103 (7.77%)<br>9    | 1 / 23 (4.35%)<br>1 |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                     | 6 / 103 (5.83%)<br>6    | 0 / 23 (0.00%)<br>0 |  |
| Cardiac disorders  |                         |                     |  |
| Extrasystoles<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 103 (0.00%)<br>0    | 2 / 23 (8.70%)<br>2 |  |
| Nervous system disorders   |                         |                     |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                            | 7 / 103 (6.80%)<br>7    | 1 / 23 (4.35%)<br>1 |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                             | 14 / 103 (13.59%)<br>14 | 1 / 23 (4.35%)<br>1 |  |
| Blood and lymphatic system disorders   |                         |                     |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                              | 7 / 103 (6.80%)<br>8    | 2 / 23 (8.70%)<br>2 |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                          | 16 / 103 (15.53%)<br>21 | 2 / 23 (8.70%)<br>4 |  |
| Thrombocytopenia   |                         |                     |  |

|  |                      |                     |  |
|--|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 7 / 103 (6.80%)<br>7 | 1 / 23 (4.35%)<br>1 |  |
| Gastrointestinal disorders                       |                      |                     |  |
| Abdominal pain                                   |                      |                     |  |
| subjects affected / exposed                      | 9 / 103 (8.74%)      | 0 / 23 (0.00%)      |  |
| occurrences (all)                                | 12                   | 0                   |  |
| Constipation                                     |                      |                     |  |
| subjects affected / exposed                      | 11 / 103 (10.68%)    | 1 / 23 (4.35%)      |  |
| occurrences (all)                                | 11                   | 1                   |  |
| Diarrhoea  |                      |                     |  |
| subjects affected / exposed                      | 45 / 103 (43.69%)    | 3 / 23 (13.04%)     |  |
| occurrences (all)                                | 75                   | 5                   |  |
| Nausea   |                      |                     |  |
| subjects affected / exposed                      | 28 / 103 (27.18%)    | 8 / 23 (34.78%)     |  |
| occurrences (all)                                | 34                   | 8                   |  |
| Vomiting   |                      |                     |  |
| subjects affected / exposed                      | 9 / 103 (8.74%)      | 3 / 23 (13.04%)     |  |
| occurrences (all)                                | 10                   | 4                   |  |
| Skin and subcutaneous tissue disorders           |                      |                     |  |
| Pruritus   |                      |                     |  |
| subjects affected / exposed                      | 3 / 103 (2.91%)      | 4 / 23 (17.39%)     |  |
| occurrences (all)                                | 5                    | 6                   |  |
| Rash maculo-papular                              |                      |                     |  |
| subjects affected / exposed                      | 7 / 103 (6.80%)      | 1 / 23 (4.35%)      |  |
| occurrences (all)                                | 7                    | 1                   |  |
| Rash   |                      |                     |  |
| subjects affected / exposed                      | 15 / 103 (14.56%)    | 6 / 23 (26.09%)     |  |
| occurrences (all)                                | 18                   | 8                   |  |
| Musculoskeletal and connective tissue disorders  |                      |                     |  |
| Arthralgia                                       |                      |                     |  |
| subjects affected / exposed                      | 16 / 103 (15.53%)    | 2 / 23 (8.70%)      |  |
| occurrences (all)                                | 17                   | 2                   |  |
| Back pain  |                      |                     |  |
| subjects affected / exposed                      | 9 / 103 (8.74%)      | 1 / 23 (4.35%)      |  |
| occurrences (all)                                | 9                    | 1                   |  |
| Myalgia  |                      |                     |  |

|  |                         |                      |  |
|--|-------------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 5 / 103 (4.85%)<br>5    | 2 / 23 (8.70%)<br>2  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)  | 8 / 103 (7.77%)<br>8    | 1 / 23 (4.35%)<br>1  |  |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)                  | 10 / 103 (9.71%)<br>12  | 1 / 23 (4.35%)<br>1  |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                  | 6 / 103 (5.83%)<br>6    | 3 / 23 (13.04%)<br>3 |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 7 / 103 (6.80%)<br>8    | 3 / 23 (13.04%)<br>4 |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 12 / 103 (11.65%)<br>13 | 2 / 23 (8.70%)<br>2  |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)   | 7 / 103 (6.80%)<br>8    | 2 / 23 (8.70%)<br>3  |  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)   | 13 / 103 (12.62%)<br>16 | 1 / 23 (4.35%)<br>1  |  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)  | 10 / 103 (9.71%)<br>12  | 0 / 23 (0.00%)<br>0  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 15 March 2017     | The primary purpose of this amendment was to align the visit schedule nomenclature with other CITADEL protocols.   |
| 15 August 2017    | The primary purpose of this amendment was to address changes requested by the European Regulatory Agency.  |
| 11 September 2017 | The primary purpose of this amendment was to address changes requested by the European Regulatory Agency.  |
| 25 October 2017   | The primary purpose of this amendment was to remove the comparator arm (idelalisib) from the study.  |
| 11 July 2018      | The primary purpose of this amendment was to modify the dose reduction schedules.  |
| 04 September 2018 | The primary purpose of this amendment was to provide a list of CYP3A inhibitors and inducers.  |
| 06 December 2018  | The primary purpose of the amendment was to stop the 1:1 allocation of participants after the 50th participant was enrolled and to enroll the remaining 50 participants to only 1 of the 2 treatment regimens being evaluated.                                     |
| 23 December 2019  | The primary purpose of this amendment was to provide additional guidance on dose modification in the event of diarrhea and colitis and to define the end of the study, including the option to receive continued treatment with INCB050465 in a rollover protocol. |
| 07 September 2022 | The primary purpose of this amendment was to describe risks associated with COVID-19.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported