



## Clinical trial results:

**A randomized, open-label, phase I/II open platform study evaluating safety and efficacy of novel ruxolitinib combinations in myelofibrosis patients**

### Summary

|                          |                            |
|--------------------------|----------------------------|
| EudraCT number           | 2019-000373-23             |
| Trial protocol           | DK DE BE NL IT ES HU AT RO |
| Global end of trial date | 28 August 2024             |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 06 August 2025 |
| First version publication date | 06 August 2025 |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CINC424H12201 |
|-----------------------|---------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04097821 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                           |
|------------------------------|-------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Novartis Pharma AG                                                                        |
| Sponsor organisation address | Novartis Campus, Basel, Switzerland,                                                      |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 28 August 2024 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 28 August 2024 |
| Was the trial ended prematurely?                     | Yes            |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to characterize the safety, tolerability, and recommended Phase 2 dose (RP2D) of each combination partner used with ruxolitinib (Part 1 core). Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 26 September 2019 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Australia: 9          |
| Country: Number of subjects enrolled | Canada: 2             |
| Country: Number of subjects enrolled | Denmark: 2            |
| Country: Number of subjects enrolled | Germany: 14           |
| Country: Number of subjects enrolled | Hungary: 2            |
| Country: Number of subjects enrolled | Italy: 2              |
| Country: Number of subjects enrolled | Netherlands: 1        |
| Country: Number of subjects enrolled | Russian Federation: 2 |
| Country: Number of subjects enrolled | Spain: 6              |
| Country: Number of subjects enrolled | Sweden: 1             |
| Country: Number of subjects enrolled | Switzerland: 2        |
| Country: Number of subjects enrolled | Türkiye: 1            |
| Country: Number of subjects enrolled | United Kingdom: 1     |
| Worldwide total number of subjects   | 45                    |
| EEA total number of subjects         | 28                    |

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)                      | 18 |
| From 65 to 84 years                       | 26 |
| 85 years and over                         | 1  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

All inclusion and exclusion criteria were checked at screening.

### 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>             | Part 1: Ruxolitinib + Siremadlin 20 mg |

Arm description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Siremadlin   |
| Investigational medicinal product code |              |
| Other name                             | HDM201       |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

10 mg, 20 mg, or 40 mg capsules for oral use

|                                        |                |
|----------------------------------------|----------------|
| Investigational medicinal product name | Ruxolitinib    |
| Investigational medicinal product code |                |
| Other name                             | INC424, Jakavi |
| Pharmaceutical forms                   | Tablet         |
| Routes of administration               | Oral use       |

Dosage and administration details:

5 mg tablets for oral use

|                  |                                        |
|------------------|----------------------------------------|
| <b>Arm title</b> | Part 1: Ruxolitinib + Siremadlin 30 mg |
|------------------|----------------------------------------|

Arm description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Siremadlin   |
| Investigational medicinal product code |              |
| Other name                             | HDM201       |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

10 mg, 20 mg, or 40 mg capsules for oral use

|                                        |                |
|----------------------------------------|----------------|
| Investigational medicinal product name | Ruxolitinib    |
| Investigational medicinal product code |                |
| Other name                             | INC424, Jakavi |
| Pharmaceutical forms                   | Tablet         |
| Routes of administration               | Oral use       |

Dosage and administration details:

5 mg tablets for oral use

|                  |                                        |
|------------------|----------------------------------------|
| <b>Arm title</b> | Part 1: Ruxolitinib + Siremadlin 40 mg |
|------------------|----------------------------------------|

Arm description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Siremadlin   |
| Investigational medicinal product code |              |
| Other name                             | HDM201       |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

10 mg, 20 mg, or 40 mg capsules for oral use

|                                        |                |
|----------------------------------------|----------------|
| Investigational medicinal product name | Ruxolitinib    |
| Investigational medicinal product code |                |
| Other name                             | INC424, Jakavi |
| Pharmaceutical forms                   | Tablet         |
| Routes of administration               | Oral use       |

Dosage and administration details:

5 mg tablets for oral use

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Part 1: Ruxolitinib + Rineterkib 200 mg |
|------------------|-----------------------------------------|

Arm description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Rineterkib   |
| Investigational medicinal product code |              |
| Other name                             | LTT462       |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

100 mg capsule for oral use

|                                        |                |
|----------------------------------------|----------------|
| Investigational medicinal product name | Ruxolitinib    |
| Investigational medicinal product code |                |
| Other name                             | INC424, Jakavi |
| Pharmaceutical forms                   | Tablet         |
| Routes of administration               | Oral use       |

Dosage and administration details:

5 mg tablets for oral use

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Part 1: Ruxolitinib + Crizanlizumab |
|------------------|-------------------------------------|

Arm description:

Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Crizanlizumab                         |
| Investigational medicinal product code |                                       |
| Other name                             | SEG101                                |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

|                                                                                                             |                                       |
|-------------------------------------------------------------------------------------------------------------|---------------------------------------|
| Dosage and administration details:<br>100 mg/10 mL concentrate for infusion for intravenous use             |                                       |
| Investigational medicinal product name                                                                      | Ruxolitinib                           |
| Investigational medicinal product code                                                                      |                                       |
| Other name                                                                                                  | INC424, Jakavi                        |
| Pharmaceutical forms                                                                                        | Tablet                                |
| Routes of administration                                                                                    | Oral use                              |
| Dosage and administration details:<br>5 mg tablets for oral use                                             |                                       |
| <b>Arm title</b>                                                                                            | Part 1: Ruxolitinib + Sabatolimab     |
| Arm description:<br>Safety run-in of sabatolimab added to existing stable dose of ruxolitinib               |                                       |
| Arm type                                                                                                    | Experimental                          |
| Investigational medicinal product name                                                                      | Sabatolimab                           |
| Investigational medicinal product code                                                                      |                                       |
| Other name                                                                                                  | MBG453                                |
| Pharmaceutical forms                                                                                        | Concentrate for solution for infusion |
| Routes of administration                                                                                    | Intravenous use                       |
| Dosage and administration details:<br>100 mg/mL or 400 mg/4 mL concentrate for infusion for intravenous use |                                       |
| Investigational medicinal product name                                                                      | Ruxolitinib                           |
| Investigational medicinal product code                                                                      |                                       |
| Other name                                                                                                  | INC424, Jakavi                        |
| Pharmaceutical forms                                                                                        | Tablet                                |
| Routes of administration                                                                                    | Oral use                              |
| Dosage and administration details:<br>5 mg tablets for oral use                                             |                                       |
| <b>Arm title</b>                                                                                            | Part 1: Ruxolitinib + NIS793          |
| Arm description:<br>Safety run-in of NIS793 added to existing stable dose of ruxolitinib                    |                                       |
| Arm type                                                                                                    | Experimental                          |
| Investigational medicinal product name                                                                      | NIS793                                |
| Investigational medicinal product code                                                                      |                                       |
| Other name                                                                                                  |                                       |
| Pharmaceutical forms                                                                                        | Concentrate for solution for infusion |
| Routes of administration                                                                                    | Intravenous use                       |
| Dosage and administration details:<br>700 mg/7 mL concentrate for infusion for intravenous use              |                                       |
| Investigational medicinal product name                                                                      | Ruxolitinib                           |
| Investigational medicinal product code                                                                      |                                       |
| Other name                                                                                                  | INC424, Jakavi                        |
| Pharmaceutical forms                                                                                        | Tablet                                |
| Routes of administration                                                                                    | Oral use                              |
| Dosage and administration details:<br>5 mg tablets for oral use                                             |                                       |
| <b>Arm title</b>                                                                                            | Part 2: Ruxolitinib                   |
| Arm description:<br>Existing stable dose of ruxolitinib as control for Part 2                               |                                       |
| Arm type                                                                                                    | Active comparator                     |

|                                        |                |
|----------------------------------------|----------------|
| Investigational medicinal product name | Ruxolitinib    |
| Investigational medicinal product code |                |
| Other name                             | INC424, Jakavi |
| Pharmaceutical forms                   | Tablet         |
| Routes of administration               | Oral use       |

Dosage and administration details:

5 mg tablets for oral use

| Number of subjects in period 1   | Part 1: Ruxolitinib + Siremadlin 20 mg | Part 1: Ruxolitinib + Siremadlin 30 mg | Part 1: Ruxolitinib + Siremadlin 40 mg |
|----------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Started                          | 7                                      | 10                                     | 6                                      |
| Completed                        | 5                                      | 8                                      | 2                                      |
| Not completed                    | 2                                      | 2                                      | 4                                      |
| Adverse event, serious fatal     | -                                      | -                                      | 3                                      |
| Physician decision               | 1                                      | 1                                      | -                                      |
| Subject Decision                 | -                                      | -                                      | -                                      |
| Adverse event, non-fatal         | -                                      | -                                      | -                                      |
| Treated in Extension Phase       | 1                                      | 1                                      | 1                                      |
| New Therapy For Study Indication | -                                      | -                                      | -                                      |

| Number of subjects in period 1   | Part 1: Ruxolitinib + Rineterkib 200 mg | Part 1: Ruxolitinib + Crizanlizumab | Part 1: Ruxolitinib + Sabatolimab |
|----------------------------------|-----------------------------------------|-------------------------------------|-----------------------------------|
| Started                          | 9                                       | 6                                   | 2                                 |
| Completed                        | 5                                       | 4                                   | 0                                 |
| Not completed                    | 4                                       | 2                                   | 2                                 |
| Adverse event, serious fatal     | 1                                       | -                                   | -                                 |
| Physician decision               | -                                       | -                                   | -                                 |
| Subject Decision                 | 1                                       | 2                                   | 2                                 |
| Adverse event, non-fatal         | 1                                       | -                                   | -                                 |
| Treated in Extension Phase       | 1                                       | -                                   | -                                 |
| New Therapy For Study Indication | -                                       | -                                   | -                                 |

| Number of subjects in period 1   | Part 1: Ruxolitinib + NIS793 | Part 2: Ruxolitinib |
|----------------------------------|------------------------------|---------------------|
| Started                          | 4                            | 1                   |
| Completed                        | 3                            | 0                   |
| Not completed                    | 1                            | 1                   |
| Adverse event, serious fatal     | -                            | -                   |
| Physician decision               | -                            | -                   |
| Subject Decision                 | -                            | 1                   |
| Adverse event, non-fatal         | -                            | -                   |
| Treated in Extension Phase       | -                            | -                   |
| New Therapy For Study Indication | 1                            | -                   |





## Baseline characteristics

### Reporting groups

|                                                                             |                                         |
|-----------------------------------------------------------------------------|-----------------------------------------|
| Reporting group title                                                       | Part 1: Ruxolitinib + Siremadlin 20 mg  |
| Reporting group description:                                                |                                         |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                         |
| Reporting group title                                                       | Part 1: Ruxolitinib + Siremadlin 30 mg  |
| Reporting group description:                                                |                                         |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                         |
| Reporting group title                                                       | Part 1: Ruxolitinib + Siremadlin 40 mg  |
| Reporting group description:                                                |                                         |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                         |
| Reporting group title                                                       | Part 1: Ruxolitinib + Rineterkib 200 mg |
| Reporting group description:                                                |                                         |
| Dose escalation of rineterkib added to existing stable dose of ruxolitinib  |                                         |
| Reporting group title                                                       | Part 1: Ruxolitinib + Crizanlizumab     |
| Reporting group description:                                                |                                         |
| Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib |                                         |
| Reporting group title                                                       | Part 1: Ruxolitinib + Sabatolimab       |
| Reporting group description:                                                |                                         |
| Safety run-in of sabatolimab added to existing stable dose of ruxolitinib   |                                         |
| Reporting group title                                                       | Part 1: Ruxolitinib + NIS793            |
| Reporting group description:                                                |                                         |
| Safety run-in of NIS793 added to existing stable dose of ruxolitinib        |                                         |
| Reporting group title                                                       | Part 2: Ruxolitinib                     |
| Reporting group description:                                                |                                         |
| Existing stable dose of ruxolitinib as control for Part 2                   |                                         |

| Reporting group values                        | Part 1: Ruxolitinib + Siremadlin 20 mg | Part 1: Ruxolitinib + Siremadlin 30 mg | Part 1: Ruxolitinib + Siremadlin 40 mg |
|-----------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Number of subjects                            | 7                                      | 10                                     | 6                                      |
| Age Categorical<br>Units: participants        |                                        |                                        |                                        |
| <65                                           | 1                                      | 5                                      | 1                                      |
| >=65                                          | 6                                      | 5                                      | 5                                      |
| Age Continuous<br>Units: years                |                                        |                                        |                                        |
| arithmetic mean                               | 70.6                                   | 62.3                                   | 74.3                                   |
| standard deviation                            | ± 6.5                                  | ± 10.7                                 | ± 9.9                                  |
| Sex: Female, Male<br>Units: participants      |                                        |                                        |                                        |
| Female                                        | 2                                      | 6                                      | 0                                      |
| Male                                          | 5                                      | 4                                      | 6                                      |
| Race/Ethnicity, Customized<br>Units: Subjects |                                        |                                        |                                        |
| White                                         | 7                                      | 10                                     | 6                                      |
| Unknown                                       | 0                                      | 0                                      | 0                                      |

| Reporting group values | Part 1: Ruxolitinib + Rineterkib 200 mg | Part 1: Ruxolitinib + Crizanlizumab | Part 1: Ruxolitinib + Sabatolimab |
|------------------------|-----------------------------------------|-------------------------------------|-----------------------------------|
|------------------------|-----------------------------------------|-------------------------------------|-----------------------------------|

|                            |       |       |        |
|----------------------------|-------|-------|--------|
| Number of subjects         | 9     | 6     | 2      |
| Age Categorical            |       |       |        |
| Units: participants        |       |       |        |
| <65                        | 4     | 4     | 1      |
| >=65                       | 5     | 2     | 1      |
| Age Continuous             |       |       |        |
| Units: years               |       |       |        |
| arithmetic mean            | 67.3  | 65.0  | 62.5   |
| standard deviation         | ± 7.8 | ± 8.1 | ± 12.0 |
| Sex: Female, Male          |       |       |        |
| Units: participants        |       |       |        |
| Female                     | 2     | 1     | 0      |
| Male                       | 7     | 5     | 2      |
| Race/Ethnicity, Customized |       |       |        |
| Units: Subjects            |       |       |        |
| White                      | 8     | 5     | 2      |
| Unknown                    | 1     | 1     | 0      |

| <b>Reporting group values</b> | Part 1: Ruxolitinib + NIS793 | Part 2: Ruxolitinib | Total |
|-------------------------------|------------------------------|---------------------|-------|
| Number of subjects            | 4                            | 1                   | 45    |
| Age Categorical               |                              |                     |       |
| Units: participants           |                              |                     |       |
| <65                           | 1                            | 1                   | 18    |
| >=65                          | 3                            | 0                   | 27    |
| Age Continuous                |                              |                     |       |
| Units: years                  |                              |                     |       |
| arithmetic mean               | 70.8                         | 58.0                |       |
| standard deviation            | ± 7.3                        | ± 0                 | -     |
| Sex: Female, Male             |                              |                     |       |
| Units: participants           |                              |                     |       |
| Female                        | 1                            | 1                   | 13    |
| Male                          | 3                            | 0                   | 32    |
| Race/Ethnicity, Customized    |                              |                     |       |
| Units: Subjects               |                              |                     |       |
| White                         | 4                            | 1                   | 43    |
| Unknown                       | 0                            | 0                   | 2     |

## End points

### End points reporting groups

|                                                                             |                                                                |
|-----------------------------------------------------------------------------|----------------------------------------------------------------|
| Reporting group title                                                       | Part 1: Ruxolitinib + Siremadlin 20 mg                         |
| Reporting group description:                                                |                                                                |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                                                |
| Reporting group title                                                       | Part 1: Ruxolitinib + Siremadlin 30 mg                         |
| Reporting group description:                                                |                                                                |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                                                |
| Reporting group title                                                       | Part 1: Ruxolitinib + Siremadlin 40 mg                         |
| Reporting group description:                                                |                                                                |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                                                |
| Reporting group title                                                       | Part 1: Ruxolitinib + Rineterkib 200 mg                        |
| Reporting group description:                                                |                                                                |
| Dose escalation of rineterkib added to existing stable dose of ruxolitinib  |                                                                |
| Reporting group title                                                       | Part 1: Ruxolitinib + Crizanlizumab                            |
| Reporting group description:                                                |                                                                |
| Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib |                                                                |
| Reporting group title                                                       | Part 1: Ruxolitinib + Sabatolimab                              |
| Reporting group description:                                                |                                                                |
| Safety run-in of sabatolimab added to existing stable dose of ruxolitinib   |                                                                |
| Reporting group title                                                       | Part 1: Ruxolitinib + NIS793                                   |
| Reporting group description:                                                |                                                                |
| Safety run-in of NIS793 added to existing stable dose of ruxolitinib        |                                                                |
| Reporting group title                                                       | Part 2: Ruxolitinib                                            |
| Reporting group description:                                                |                                                                |
| Existing stable dose of ruxolitinib as control for Part 2                   |                                                                |
| Subject analysis set title                                                  | Part 1:Ruxolitinib + Siremadlin 20 mg (AUClast for Siremadlin) |
| Subject analysis set type                                                   | Sub-group analysis                                             |
| Subject analysis set description:                                           |                                                                |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                                                |
| Subject analysis set title                                                  | Part 1:Ruxolitinib + Siremadlin 30 mg (AUClast for Siremadlin) |
| Subject analysis set type                                                   | Sub-group analysis                                             |
| Subject analysis set description:                                           |                                                                |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                                                |
| Subject analysis set title                                                  | Part 1:Ruxolitinib + Siremadlin 40 mg (AUClast for Siremadlin) |
| Subject analysis set type                                                   | Sub-group analysis                                             |
| Subject analysis set description:                                           |                                                                |
| Dose escalation of siremadlin added to existing stable dose of ruxolitinib  |                                                                |
| Subject analysis set title                                                  | Part 1:Ruxolitinib+ Rineterkib 200 mg (AUClast for Rineterkib) |
| Subject analysis set type                                                   | Sub-group analysis                                             |
| Subject analysis set description:                                           |                                                                |
| Dose escalation of rineterkib added to existing stable dose of ruxolitinib  |                                                                |
| Subject analysis set title                                                  | Part 1:Ruxolitinib + Crizanlizumab (AUClast for Crizanlizumab) |
| Subject analysis set type                                                   | Sub-group analysis                                             |
| Subject analysis set description:                                           |                                                                |
| Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib |                                                                |
| Subject analysis set title                                                  | Part 1: Ruxolitinib + Sabatolimab (AUClast for Sabatolimab)    |
| Subject analysis set type                                                   | Sub-group analysis                                             |

Subject analysis set description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

|                            |                                                   |
|----------------------------|---------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + NIS793 (AUClast for NIS793) |
| Subject analysis set type  | Sub-group analysis                                |

Subject analysis set description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Siremadlin 20 mg (Cmax for Siremadlin) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Siremadlin 30 mg (Cmax for Siremadlin) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Siremadlin 40 mg (Cmax for Siremadlin) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                            |                                                               |
|----------------------------|---------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Rineterkib 200 mg (Cmax for Rineterkib) |
| Subject analysis set type  | Sub-group analysis                                            |

Subject analysis set description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Crizanlizumab (Cmax for Crizanlizumab) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib

|                            |                                                          |
|----------------------------|----------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Sabatolimab (Cmax for Sabatolimab) |
| Subject analysis set type  | Sub-group analysis                                       |

Subject analysis set description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

|                            |                                                |
|----------------------------|------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + NIS793 (Cmax for NIS793) |
| Subject analysis set type  | Sub-group analysis                             |

Subject analysis set description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Siremadlin 20 mg (Tmax for Siremadlin) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Siremadlin 30 mg (Tmax for Siremadlin) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Siremadlin 40 mg (Tmax for Siremadlin) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                            |                                                               |
|----------------------------|---------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Rineterkib 200 mg (Tmax for Rineterkib) |
| Subject analysis set type  | Sub-group analysis                                            |

Subject analysis set description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

|                            |                                                              |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Crizanlizumab (Tmax for Crizanlizumab) |
| Subject analysis set type  | Sub-group analysis                                           |

Subject analysis set description:

Safety run-in of crizanolizumab added to existing stable dose of ruxolitinib

|                            |                                                          |
|----------------------------|----------------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + Sabatolimab (Tmax for Sabatolimab) |
| Subject analysis set type  | Sub-group analysis                                       |

Subject analysis set description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

|                            |                                                |
|----------------------------|------------------------------------------------|
| Subject analysis set title | Part 1: Ruxolitinib + NIS793 (Tmax for NIS793) |
| Subject analysis set type  | Sub-group analysis                             |

Subject analysis set description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

### **Primary: Incidence and Severity of Dose Limiting Toxicities Within the First 2 Cycles in Part 1**

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Incidence and Severity of Dose Limiting Toxicities Within the First 2 Cycles in Part 1 <sup>[1][2]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------|

End point description:

Incidence and severity of dose limiting toxicities within the first 2 cycles (6 or 8 weeks) in Part 1 of the study. DLTs were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) criteria Version 5.0. Grade 0 was assigned for all non-missing values not graded as 1 or higher. Higher grade indicated more severity. Grade 5 was not used.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to the end of Cycle 2 (6 or 8 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: No statistical analysis was planned for this primary outcome.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values            | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type          | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed | 6                                               | 7                                               | 5                                               | 9                                                |
| Units: participants         |                                                 |                                                 |                                                 |                                                  |
| Grade 3                     | 0                                               | 0                                               | 1                                               | 1                                                |
| Grade 4                     | 0                                               | 1                                               | 1                                               | 0                                                |

| End point values            | Part 1:<br>Ruxolitinib +<br>Crizanolizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------|--------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type          | Reporting group                            | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed | 5                                          | 2                                       | 0 <sup>[3]</sup>                   |  |
| Units: participants         |                                            |                                         |                                    |  |
| Grade 3                     | 0                                          | 0                                       |                                    |  |
| Grade 4                     | 0                                          | 0                                       |                                    |  |

Notes:

[3] - Number analyzed is the number of participants with available data.

## Statistical analyses

No statistical analyses for this end point

### Primary: Response Rate at the End of Cycle 6 or Cycle 8 in Part 1

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Response Rate at the End of Cycle 6 or Cycle 8 in Part 1 <sup>[4][5]</sup> |
|-----------------|----------------------------------------------------------------------------|

End point description:

Composite of anemia improvement (hemoglobin level) and no spleen volume progression and no symptom worsening in Part 2 and Part 3 of the study. For a subject to be considered a responder, all three components of the composite had to be fulfilled.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to the end of Cycle 6 or 8 (24 weeks)

Notes:

[4] - 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: No statistical analysis was planned for this primary outcome.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                  | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed       | 0 <sup>[6]</sup>                                | 0 <sup>[7]</sup>                                | 0 <sup>[8]</sup>                                | 0 <sup>[9]</sup>                                 |
| Units: percentage of participants |                                                 |                                                 |                                                 |                                                  |

Notes:

[6] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[7] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[8] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[9] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

| End point values                  | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed       | 0 <sup>[10]</sup>                         | 0 <sup>[11]</sup>                       | 0 <sup>[12]</sup>                  |  |
| Units: percentage of participants |                                           |                                         |                                    |  |

Notes:

[10] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[11] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

[12] - Enrollment was permanently halted; therefore, data were not collected for this outcome measure.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Achieving an Improvement in Hemoglobin Level of $\geq 1.5$ g/dL From Baseline in Part 1

|                 |                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects Achieving an Improvement in Hemoglobin Level of $\geq 1.5$ g/dL From Baseline in Part 1 <sup>[13]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Week 24, Week 48

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                  | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed       | 7                                               | 10                                              | 6                                               | 9                                                |
| Units: percentage of participants |                                                 |                                                 |                                                 |                                                  |
| number (not applicable)           |                                                 |                                                 |                                                 |                                                  |
| Week 24                           | 0                                               | 0                                               | 0                                               | 11.1                                             |
| Week 48                           | 0                                               | 0                                               | 0                                               | 11.1                                             |

| End point values                  | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed       | 6                                         | 2                                       | 4                                  |  |
| Units: percentage of participants |                                           |                                         |                                    |  |
| number (not applicable)           |                                           |                                         |                                    |  |
| Week 24                           | 16.7                                      | 0                                       | 0                                  |  |
| Week 48                           | 0                                         | 0                                       | 0                                  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Achieving an Improvement in Hemoglobin Level of at Least $\geq 2.0$ g/dL From Baseline in Part 1

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects Achieving an Improvement in Hemoglobin Level of at Least $\geq 2.0$ g/dL From Baseline in Part 1 <sup>[14]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

|                                                                                                                                                                                                                          |           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                                                                                                                           | Secondary |
| End point timeframe:                                                                                                                                                                                                     |           |
| Week 24, Week 48                                                                                                                                                                                                         |           |
| Notes:                                                                                                                                                                                                                   |           |
| [14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. |           |
| Justification: Applicable to Part 1 only.                                                                                                                                                                                |           |

| End point values                  | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed       | 7                                               | 10                                              | 6                                               | 9                                                |
| Units: percentage of participants |                                                 |                                                 |                                                 |                                                  |
| number (not applicable)           |                                                 |                                                 |                                                 |                                                  |
| Week 24                           | 0                                               | 0                                               | 0                                               | 11.1                                             |
| Week 48                           | 0                                               | 0                                               | 0                                               | 11.1                                             |

| End point values                  | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed       | 6                                         | 2                                       | 4                                  |  |
| Units: percentage of participants |                                           |                                         |                                    |  |
| number (not applicable)           |                                           |                                         |                                    |  |
| Week 24                           | 0                                         | 0                                       | 0                                  |  |
| Week 48                           | 0                                         | 0                                       | 0                                  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Spleen Length From Baseline in Part 1

|                                                                                                                                                                                                                          |                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|
| End point title                                                                                                                                                                                                          | Change in Spleen Length From Baseline in Part 1 <sup>[15]</sup> |
| End point description:                                                                                                                                                                                                   |                                                                 |
| Change in spleen length measured in centimeters by manual palpation.                                                                                                                                                     |                                                                 |
| End point type                                                                                                                                                                                                           | Secondary                                                       |
| End point timeframe:                                                                                                                                                                                                     |                                                                 |
| Baseline, Week 24, Week 48                                                                                                                                                                                               |                                                                 |
| Notes:                                                                                                                                                                                                                   |                                                                 |
| [15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. |                                                                 |
| Justification: Applicable to Part 1 only.                                                                                                                                                                                |                                                                 |



| End point values                     | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|--------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                   | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed          | 6                                               | 8                                               | 4                                               | 4                                                |
| Units: centimeters                   |                                                 |                                                 |                                                 |                                                  |
| arithmetic mean (standard deviation) |                                                 |                                                 |                                                 |                                                  |
| Week 24 n=6,8,4,4,4,0,0              | -3.3 (± 2.6)                                    | -5.5 (± 3.9)                                    | -6.3 (± 4.6)                                    | -1.8 (± 3.9)                                     |
| Week 48 n=2,1,2,1,1,0,0              | -5.0 (± 0.0)                                    | -9.0 (± 999)                                    | -6.0 (± 7.1)                                    | -8.0 (± 999)                                     |

| End point values                     | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|--------------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                   | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed          | 4                                         | 0 <sup>[16]</sup>                       | 0 <sup>[17]</sup>                  |  |
| Units: centimeters                   |                                           |                                         |                                    |  |
| arithmetic mean (standard deviation) |                                           |                                         |                                    |  |
| Week 24 n=6,8,4,4,4,0,0              | -1.5 (± 1.9)                              | ()                                      | ()                                 |  |
| Week 48 n=2,1,2,1,1,0,0              | -5.0 (± 999)                              | ()                                      | ()                                 |  |

Notes:

[16] - Number analyzed is the number of participants with available data.

[17] - Number analyzed is the number of participants with available data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With $\geq 35\%$ Reduction in Spleen Volume From Baseline in Part 1

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects With $\geq 35\%$ Reduction in Spleen Volume From Baseline in Part 1 <sup>[18]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------|

End point description:

Change in spleen volume measured by magnetic resonance imaging (MRI) or computed tomography (CT) from baseline.

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

End point timeframe:

Week 24, Week 48

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                  | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed       | 7                                               | 10                                              | 6                                               | 9                                                |
| Units: percentage of participants |                                                 |                                                 |                                                 |                                                  |
| number (not applicable)           |                                                 |                                                 |                                                 |                                                  |
| Week 24                           | 14.3                                            | 60.0                                            | 0                                               | 0                                                |

|         |      |      |      |   |
|---------|------|------|------|---|
| Week 48 | 14.3 | 10.0 | 16.7 | 0 |
|---------|------|------|------|---|

| End point values                  | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed       | 6                                         | 2                                       | 4                                  |  |
| Units: percentage of participants |                                           |                                         |                                    |  |
| number (not applicable)           |                                           |                                         |                                    |  |
| Week 24                           | 0                                         | 0                                       | 0                                  |  |
| Week 48                           | 0                                         | 0                                       | 0                                  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With $\geq 25\%$ Reduction in Spleen Volume From Baseline in Part 1

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects With $\geq 25\%$ Reduction in Spleen Volume From Baseline in Part 1 <sup>[19]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------|

End point description:

Change in spleen volume measured by magnetic resonance imaging (MRI) or computed tomography (CT) from baseline.

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

End point timeframe:

Week 24, Week 48

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                  | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed       | 7                                               | 10                                              | 6                                               | 9                                                |
| Units: percentage of participants |                                                 |                                                 |                                                 |                                                  |
| number (not applicable)           |                                                 |                                                 |                                                 |                                                  |
| Week 24                           | 28.6                                            | 60.0                                            | 0                                               | 11.1                                             |
| Week 48                           | 28.6                                            | 10.0                                            | 16.7                                            | 11.1                                             |

| End point values | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
|------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|

|                                   |                 |                 |                 |  |
|-----------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type                | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed       | 6               | 2               | 4               |  |
| Units: percentage of participants |                 |                 |                 |  |
| number (not applicable)           |                 |                 |                 |  |
| Week 24                           | 0               | 0               | 0               |  |
| Week 48                           | 0               | 0               | 0               |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects in Part 1 With $\geq 50\%$ Reduction From Baseline in Myelofibrosis Symptom Assessment Form, Version 4.0 (MFSAF v4.0)

|                 |                                                                                                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects in Part 1 With $\geq 50\%$ Reduction From Baseline in Myelofibrosis Symptom Assessment Form, Version 4.0 (MFSAF v4.0) <sup>[20]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The MFSAF v4.0 questionnaire focuses on the 7 core symptoms of MF: fatigue, night sweats, pruritus, abdominal discomfort, pain under the ribs on the left side, early satiety and bone pain. Subjects record symptom severity at it worst for each of the 7 symptoms on an 11-point numeric rating scale, from 0 (absent) to 10 (worst imaginable). The Total Symptom Score (TSS) is the sum of all the scores for all 7 symptoms.

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

End point timeframe:

Week 12, Week 24, Week 48

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                  | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed       | 7                                               | 10                                              | 6                                               | 9                                                |
| Units: percentage of participants |                                                 |                                                 |                                                 |                                                  |
| number (not applicable)           |                                                 |                                                 |                                                 |                                                  |
| Week 12                           | 42.9                                            | 30.0                                            | 16.7                                            | 11.1                                             |
| Week 24                           | 14.3                                            | 20.0                                            | 33.3                                            | 11.1                                             |
| Week 48                           | 14.3                                            | 10.0                                            | 16.7                                            | 0                                                |

| End point values                  | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed       | 6                                         | 2                                       | 4                                  |  |
| Units: percentage of participants |                                           |                                         |                                    |  |
| number (not applicable)           |                                           |                                         |                                    |  |

|         |      |   |   |  |
|---------|------|---|---|--|
| Week 12 | 16.7 | 0 | 0 |  |
| Week 24 | 16.7 | 0 | 0 |  |
| Week 48 | 0    | 0 | 0 |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1

|                 |                                                                                                                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1 |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1 and 5 of Cycles 1 and 2 for siremadlin and Cycles 1 and 3 for crizanlizumab, sabatolimab, and NIS793; Days 1 and 15 of Cycle 1 for rineterkib

| End point values                     | Part 1:Ruxolitinib + Siremadlin 20 mg (AUClast for Siremadlin) | Part 1:Ruxolitinib + Siremadlin 30 mg (AUClast for Siremadlin) | Part 1:Ruxolitinib + Siremadlin 40 mg (AUClast for Siremadlin) | Part 1:Ruxolitinib+ Rineterkib 200 mg (AUClast for Rineterkib) |
|--------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------|
| Subject group type                   | Subject analysis set                                           | Subject analysis set                                           | Subject analysis set                                           | Subject analysis set                                           |
| Number of subjects analysed          | 6                                                              | 9                                                              | 5                                                              | 9                                                              |
| Units: ng*hr/mL                      |                                                                |                                                                |                                                                |                                                                |
| arithmetic mean (standard deviation) |                                                                |                                                                |                                                                |                                                                |
| Cycle 1 Day 1 n=6,9,5,9,5,2,4        | 1520 (± 619)                                                   | 2560 (± 1530)                                                  | 3780 (± 1840)                                                  | 6000 (± 5120)                                                  |
| Cycle 1 Day 5 n=6,7,5,0,0,0,0        | 2230 (± 1110)                                                  | 3340 (± 2120)                                                  | 4390 (± 2270)                                                  | 999 (± 999)                                                    |
| Cycle 2 Day 1 n=5,6,3,0,0,0,0        | 1720 (± 1020)                                                  | 2400 (± 1150)                                                  | 2870 (± 326)                                                   | 999 (± 999)                                                    |
| Cycle 2 Day 5 n=3,5,3,0,0,0,0        | 1590 (± 577)                                                   | 2860 (± 1680)                                                  | 3030 (± 786)                                                   | 999 (± 999)                                                    |
| Cycle 1 Day 15 n=0,0,0,9,0,0,0       | 999 (± 999)                                                    | 999 (± 999)                                                    | 999 (± 999)                                                    | 15800 (± 11000)                                                |
| Cycle 3 Day 1 n=0,0,0,0,5,2,3        | 999 (± 999)                                                    | 999 (± 999)                                                    | 999 (± 999)                                                    | 999 (± 999)                                                    |

| End point values                     | Part 1:Ruxolitinib + Crizanlizumab (AUClast for Crizanlizumab) | Part 1: Ruxolitinib + Sabatolimab (AUClast for Sabatolimab) | Part 1: Ruxolitinib + NIS793 (AUClast for NIS793) |  |
|--------------------------------------|----------------------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------|--|
| Subject group type                   | Subject analysis set                                           | Subject analysis set                                        | Subject analysis set                              |  |
| Number of subjects analysed          | 5                                                              | 2                                                           | 4                                                 |  |
| Units: ng*hr/mL                      |                                                                |                                                             |                                                   |  |
| arithmetic mean (standard deviation) |                                                                |                                                             |                                                   |  |

|                                |                       |                |                        |  |
|--------------------------------|-----------------------|----------------|------------------------|--|
| Cycle 1 Day 1 n=6,9,5,9,5,2,4  | 14100000 (± 4990000)  | 34900 (± 7860) | 103000000 (± 18700000) |  |
| Cycle 1 Day 5 n=6,7,5,0,0,0,0  | 999 (± 999)           | 999 (± 999)    | 999 (± 999)            |  |
| Cycle 2 Day 1 n=5,6,3,0,0,0,0  | 999 (± 999)           | 999 (± 999)    | 999 (± 999)            |  |
| Cycle 2 Day 5 n=3,5,3,0,0,0,0  | 999 (± 999)           | 999 (± 999)    | 999 (± 999)            |  |
| Cycle 1 Day 15 n=0,0,0,9,0,0,0 | 999 (± 999)           | 999 (± 999)    | 999 (± 999)            |  |
| Cycle 3 Day 1 n=0,0,0,0,5,2,3  | 20900000 (± 13000000) | 43500 (± 9110) | 166000000 (± 63600000) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Ruxolitinib in Part 1

|                 |                                                                                                                                                                             |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Measurable Concentration Sampling Time (AUClast) for Ruxolitinib in Part 1 <sup>[21]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1 and 5 of Cycles 1 and 2; Day 15 of Cycle 1

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                                    | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|-----------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                                  | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed                         | 3                                               | 4                                               | 2                                               | 3                                                |
| Units: ng*hr/mL                                     |                                                 |                                                 |                                                 |                                                  |
| arithmetic mean (standard deviation)                |                                                 |                                                 |                                                 |                                                  |
| Ruxolitinib 5 mg Cycle 1 Day 1<br>n=0,0,2,1,0,0,0   | 999 (± 999)                                     | 999 (± 999)                                     | 344 (± 225)                                     | 199 (± 999)                                      |
| Ruxolitinib 10 mg Cycle 1 Day 1<br>n=3,4,1,2,1,2,1  | 546 (± 412)                                     | 673 (± 290)                                     | 498 (± 999)                                     | 633 (± 393)                                      |
| Ruxolitinib 15 mg Cycle 1 Day 1<br>n=1,0,2,1,2,0,2  | 1090 (± 999)                                    | 999 (± 999)                                     | 481 (± 243)                                     | 729 (± 999)                                      |
| Ruxolitinib 20 mg Cycle 1 Day 1<br>n=3,2,1,3,1,0,0  | 991 (± 183)                                     | 616 (± 107)                                     | 623 (± 999)                                     | 913 (± 451)                                      |
| Ruxolitinib 25 mg Cycle 1 Day 1<br>n=0,0,0,1,0,0,1  | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 188 (± 999)                                      |
| Ruxolitinib 5 mg Cycle 1 Day 5<br>n=0,0,2,0,0,0,0   | 999 (± 999)                                     | 999 (± 999)                                     | 245 (± 173)                                     | 999 (± 999)                                      |
| Ruxolitinib 10 mg Cycle 1 Day 5<br>n=3,3,1,0,0,0,0, | 465 (± 228)                                     | 550 (± 307)                                     | 441 (± 999)                                     | 999 (± 999)                                      |
| Ruxolitinib 15 mg Cycle 1 Day 5<br>n=1,1,2,0,0,0,0  | 849 (± 999)                                     | 901 (± 999)                                     | 454 (± 212)                                     | 999 (± 999)                                      |

|                                                      |              |              |              |             |
|------------------------------------------------------|--------------|--------------|--------------|-------------|
| Ruxolitinib 20 mg Cycle 1 Day 5<br>n=2,4,1,0,0,0     | 872 (± 218)  | 652 (± 218)  | 482 (± 999)  | 999 (± 999) |
| Ruxolitinib 5 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0   | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 289 (± 999) |
| Ruxolitinib 10 mg Cycle 1 Day 15<br>n=0,0,0,2,0,0,0  | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 592 (± 403) |
| Ruxolitinib 15 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0, | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 518 (± 999) |
| Ruxolitinib 20 mg Cycle 1 Day 15<br>n=0,0,0,3,0,0,0  | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 957 (± 479) |
| Ruxolitinib 25 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0  | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 718 (± 999) |
| Ruxolitinib 5 mg Cycle 2 Day 1<br>n=0,0,1,0,0,0,0    | 999 (± 999)  | 999 (± 999)  | 172 (± 999)  | 999 (± 999) |
| Ruxolitinib 10 mg Cycle 2 Day 1<br>n=2,2,1,0,0,0,0   | 354 (± 101)  | 507 (± 225)  | 553 (± 999)  | 999 (± 999) |
| Ruxolitinib 15 mg Cycle 2 Day 1<br>n=1,2,2,0,0,0,0   | 1040 (± 999) | 1190 (± 214) | 334 (± 98.7) | 999 (± 999) |
| Ruxolitinib 20 mg Cycle 2 Day 1<br>n=3,3,1,0,0,0,0   | 823 (± 206)  | 727 (± 200)  | 521 (± 999)  | 999 (± 999) |

| End point values                                     | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|------------------------------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                                   | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed                          | 2                                         | 2                                       | 2                                  |  |
| Units: ng*hr/mL                                      |                                           |                                         |                                    |  |
| arithmetic mean (standard deviation)                 |                                           |                                         |                                    |  |
| Ruxolitinib 5 mg Cycle 1 Day 1<br>n=0,0,2,1,0,0,0    | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 1 Day 1<br>n=3,4,1,2,1,2,1   | 440 (± 999)                               | 336 (± 30.6)                            | 452 (± 999)                        |  |
| Ruxolitinib 15 mg Cycle 1 Day 1<br>n=1,0,2,1,2,0,2   | 662 (± 420)                               | 999 (± 999)                             | 1220 (± 637)                       |  |
| Ruxolitinib 20 mg Cycle 1 Day 1<br>n=3,2,1,3,1,0,0   | 887 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 25 mg Cycle 1 Day 1<br>n=0,0,0,1,0,0,1   | 999 (± 999)                               | 999 (± 999)                             | 859 (± 999)                        |  |
| Ruxolitinib 5 mg Cycle 1 Day 5<br>n=0,0,2,0,0,0,0    | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 1 Day 5<br>n=3,3,1,0,0,0,0,  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 15 mg Cycle 1 Day 5<br>n=1,1,2,0,0,0,0   | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 20 mg Cycle 1 Day 5<br>n=2,4,1,0,0,0,0   | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 5 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0   | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 1 Day 15<br>n=0,0,0,2,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 15 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0, | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 20 mg Cycle 1 Day 15<br>n=0,0,0,3,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 25 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 5 mg Cycle 2 Day 1<br>n=0,0,1,0,0,0,0    | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |

|                                                    |             |             |             |  |
|----------------------------------------------------|-------------|-------------|-------------|--|
| Ruxolitinib 10 mg Cycle 2 Day 1<br>n=2,2,1,0,0,0,0 | 999 (± 999) | 999 (± 999) | 999 (± 999) |  |
| Ruxolitinib 15 mg Cycle 2 Day 1<br>n=1,2,2,0,0,0,0 | 999 (± 999) | 999 (± 999) | 999 (± 999) |  |
| Ruxolitinib 20 mg Cycle 2 Day 1<br>n=3,3,1,0,0,0,0 | 999 (± 999) | 999 (± 999) | 999 (± 999) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum (Peak) Observed Plasma Drug Concentration (C<sub>max</sub>) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1

|                 |                                                                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Maximum (Peak) Observed Plasma Drug Concentration (C <sub>max</sub> ) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1 |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1 and 5 of Cycles 1 and 2 for siremadlin and Cycles 1 and 3 for crizanlizumab, sabatolimab, and NIS793; Days 1 and 15 of Cycle 1 for rineterkib

| End point values                     | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg (C <sub>max</sub> for<br>Siremadlin) | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg (C <sub>max</sub> for<br>Siremadlin) | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg (C <sub>max</sub> for<br>Siremadlin) | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg (C <sub>max</sub> for<br>Rineterkib) |
|--------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| Subject group type                   | Subject analysis set                                                                 | Subject analysis set                                                                 | Subject analysis set                                                                 | Subject analysis set                                                                  |
| Number of subjects analysed          | 6                                                                                    | 9                                                                                    | 5                                                                                    | 9                                                                                     |
| Units: ng/mL                         |                                                                                      |                                                                                      |                                                                                      |                                                                                       |
| arithmetic mean (standard deviation) |                                                                                      |                                                                                      |                                                                                      |                                                                                       |
| Cycle 1 Day 1 n=6,9,5,9,5,2,4        | 118 (± 32.8)                                                                         | 207 (± 122)                                                                          | 290 (± 56.1)                                                                         | 469 (± 358)                                                                           |
| Cycle 1 Day 5 n=6,7,5,0,0,0,0        | 161 (± 78.0)                                                                         | 284 (± 138)                                                                          | 336 (± 109)                                                                          | 999 (± 999)                                                                           |
| Cycle 2 Day 1 n=5,6,3,0,0,0,0        | 131 (± 57.9)                                                                         | 142 (± 102)                                                                          | 268 (± 15.0)                                                                         | 999 (± 999)                                                                           |
| Cycle 2 Day 5 n=3,5,3,0,0,0,0        | 103 (± 34.1)                                                                         | 193 (± 95.0)                                                                         | 228 (± 58.3)                                                                         | 999 (± 999)                                                                           |
| Cycle 1 Day 15 n=0,0,0,9,0,0,0       | 999 (± 999)                                                                          | 999 (± 999)                                                                          | 999 (± 999)                                                                          | 987 (± 621)                                                                           |
| Cycle 3 Day 1 n=0,0,0,0,5,2,3        | 999 (± 999)                                                                          | 999 (± 999)                                                                          | 999 (± 999)                                                                          | 999 (± 999)                                                                           |

| End point values                     | Part 1:<br>Ruxolitinib +<br>Crizanlizumab<br>(C <sub>max</sub> for<br>Crizanlizumab) | Part 1:<br>Ruxolitinib +<br>Sabatolimab<br>(C <sub>max</sub> for<br>Sabatolimab) | Part 1:<br>Ruxolitinib +<br>NIS793 (C <sub>max</sub><br>for NIS793) |  |
|--------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------------------|--|
| Subject group type                   | Subject analysis set                                                                 | Subject analysis set                                                             | Subject analysis set                                                |  |
| Number of subjects analysed          | 5                                                                                    | 2                                                                                | 4                                                                   |  |
| Units: ng/mL                         |                                                                                      |                                                                                  |                                                                     |  |
| arithmetic mean (standard deviation) |                                                                                      |                                                                                  |                                                                     |  |

|                                |                  |              |                   |  |
|--------------------------------|------------------|--------------|-------------------|--|
| Cycle 1 Day 1 n=6,9,5,9,5,2,4  | 114000 (± 36400) | 131 (± 17.7) | 439000 (± 56100)  |  |
| Cycle 1 Day 5 n=6,7,5,0,0,0,0  | 999 (± 999)      | 999 (± 999)  | 999 (± 999)       |  |
| Cycle 2 Day 1 n=5,6,3,0,0,0,0  | 999 (± 999)      | 999 (± 999)  | 999 (± 999)       |  |
| Cycle 2 Day 5 n=3,5,3,0,0,0,0  | 999 (± 999)      | 999 (± 999)  | 999 (± 999)       |  |
| Cycle 1 Day 15 n=0,0,0,9,0,0,0 | 999 (± 999)      | 999 (± 999)  | 999 (± 999)       |  |
| Cycle 3 Day 1 n=0,0,0,0,5,2,3  | 114000 (± 56600) | 150 (± 33.2) | 743000 (± 314000) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum (Peak) Observed Plasma Drug Concentration (Cmax) for Ruxolitinib in Part 1

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Maximum (Peak) Observed Plasma Drug Concentration (Cmax) for Ruxolitinib in Part 1 <sup>[22]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1 and 5 of Cycles 1 and 2; Day 15 of Cycle 1

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                                   | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|----------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                                 | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed                        | 3                                               | 4                                               | 2                                               | 3                                                |
| Units: ng/mL                                       |                                                 |                                                 |                                                 |                                                  |
| arithmetic mean (standard deviation)               |                                                 |                                                 |                                                 |                                                  |
| Ruxolitinib 5 mg Cycle 1 Day 1<br>n=0,0,2,1,0,0,0  | 999 (± 999)                                     | 999 (± 999)                                     | 93.3 (± 26.5)                                   | 67.4 (± 999)                                     |
| Ruxolitinib 10 mg Cycle 1 Day 1<br>n=3,4,1,2,1,2,1 | 184 (± 159)                                     | 209 (± 20.8)                                    | 108 (± 999)                                     | 195 (± 41.0)                                     |
| Ruxolitinib 15 mg Cycle 1 Day 1<br>n=1,0,2,1,2,0,2 | 334 (± 999)                                     | 999 (± 999)                                     | 119 (± 76.2)                                    | 193 (± 999)                                      |
| Ruxolitinib 20 mg Cycle 1 Day 1<br>n=3,2,1,3,1,0,0 | 310 (± 131)                                     | 184 (± 14.8)                                    | 232 (± 999)                                     | 332 (± 33.5)                                     |
| Ruxolitinib 25 mg Cycle 1 Day 1<br>n=0,0,0,1,0,0,1 | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 46.0 (± 999)                                     |
| Ruxolitinib 5 mg Cycle 1 Day 5<br>n=0,0,2,0,0,0,0  | 999 (± 999)                                     | 999 (± 999)                                     | 74.8 (± 13.5)                                   | 999 (± 999)                                      |
| Ruxolitinib 10 mg Cycle 1 Day 5<br>n=3,3,1,0,0,0,0 | 152 (± 55.3)                                    | 149 (± 67.6)                                    | 107 (± 999)                                     | 999 (± 999)                                      |
| Ruxolitinib 15 mg Cycle 1 Day 5<br>n=1,1,2,0,0,0,0 | 252 (± 999)                                     | 264 (± 999)                                     | 172 (± 96.9)                                    | 999 (± 999)                                      |
| Ruxolitinib 20 mg Cycle 1 Day 5<br>n=2,4,1,0,0,0,0 | 211 (± 48.8)                                    | 232 (± 104)                                     | 180 (± 999)                                     | 999 (± 999)                                      |



|                                                     |              |              |              |              |
|-----------------------------------------------------|--------------|--------------|--------------|--------------|
| Ruxolitinib 5 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0  | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 95.4 (± 999) |
| Ruxolitinib 10 mg Cycle 1 Day 15<br>n=0,0,0,2,0,0,0 | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 158 (± 68.6) |
| Ruxolitinib 15 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 126 (± 999)  |
| Ruxolitinib 20 mg Cycle 1 Day 15<br>n=0,0,0,3,0,0,0 | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 369 (± 83.7) |
| Ruxolitinib 25 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (± 999)  | 999 (± 999)  | 999 (± 999)  | 323 (± 999)  |
| Ruxolitinib 5 mg Cycle 2 Day 1<br>n=0,0,1,0,0,0,0   | 999 (± 999)  | 999 (± 999)  | 82.1 (± 999) | 999 (± 999)  |
| Ruxolitinib 10 mg Cycle 2 Day 1<br>n=2,2,1,0,0,0,0  | 119 (± 66.7) | 165 (± 29.7) | 90.5 (± 999) | 999 (± 999)  |
| Ruxolitinib 15 mg Cycle 2 Day 1<br>n=1,2,2,0,0,0,0  | 260 (± 999)  | 337 (± 70.7) | 100 (± 68.9) | 999 (± 999)  |
| Ruxolitinib 20 mg Cycle 2 Day 1<br>n=3,3,1,0,0,0,0  | 257 (± 71.0) | 176 (± 66.0) | 241 (± 999)  | 999 (± 999)  |

| End point values                                    | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                                  | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed                         | 2                                         | 2                                       | 2                                  |  |
| Units: ng/mL                                        |                                           |                                         |                                    |  |
| arithmetic mean (standard deviation)                |                                           |                                         |                                    |  |
| Ruxolitinib 5 mg Cycle 1 Day 1<br>n=0,0,2,1,0,0,0   | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 1 Day 1<br>n=3,4,1,2,1,2,1  | 191 (± 999)                               | 118 (± 33.0)                            | 132 (± 999)                        |  |
| Ruxolitinib 15 mg Cycle 1 Day 1<br>n=1,0,2,1,2,0,2  | 185 (± 120)                               | 999 (± 999)                             | 254 (± 73.5)                       |  |
| Ruxolitinib 20 mg Cycle 1 Day 1<br>n=3,2,1,3,1,0,0  | 221 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 25 mg Cycle 1 Day 1<br>n=0,0,0,1,0,0,1  | 999 (± 999)                               | 999 (± 999)                             | 224 (± 999)                        |  |
| Ruxolitinib 5 mg Cycle 1 Day 5<br>n=0,0,2,0,0,0,0   | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 1 Day 5<br>n=3,3,1,0,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 15 mg Cycle 1 Day 5<br>n=1,1,2,0,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 20 mg Cycle 1 Day 5<br>n=2,4,1,0,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 5 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 1 Day 15<br>n=0,0,0,2,0,0,0 | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 15 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 20 mg Cycle 1 Day 15<br>n=0,0,0,3,0,0,0 | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 25 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 5 mg Cycle 2 Day 1<br>n=0,0,1,0,0,0,0   | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Ruxolitinib 10 mg Cycle 2 Day 1<br>n=2,2,1,0,0,0,0  | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |

|                                                    |             |             |             |  |
|----------------------------------------------------|-------------|-------------|-------------|--|
| Ruxolitinib 15 mg Cycle 2 Day 1<br>n=1,2,2,0,0,0,0 | 999 (± 999) | 999 (± 999) | 999 (± 999) |  |
| Ruxolitinib 20 mg Cycle 2 Day 1<br>n=3,3,1,0,0,0,0 | 999 (± 999) | 999 (± 999) | 999 (± 999) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1

|                 |                                                                                                                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Siremadlin, Rineterkib, Crizanlizumab, Sabatolimab, and NIS793 in Part 1 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1 and 5 of Cycles 1 and 2 for siremadlin and Cycles 1 and 3 for crizanlizumab, sabatolimab, and NIS793; Days 1 and 15 of Cycle 1 for rineterkib

| End point values               | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg (Tmax for<br>Siremadlin) | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg (Tmax for<br>Siremadlin) | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg (Tmax for<br>Siremadlin) | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg (Tmax for<br>Rineterkib) |
|--------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Subject group type             | Subject analysis set                                                     | Subject analysis set                                                     | Subject analysis set                                                     | Subject analysis set                                                      |
| Number of subjects analysed    | 6                                                                        | 9                                                                        | 5                                                                        | 9                                                                         |
| Units: hours                   |                                                                          |                                                                          |                                                                          |                                                                           |
| median (full range (min-max))  |                                                                          |                                                                          |                                                                          |                                                                           |
| Cycle 1 Day 1 n=6,9,5,9,5,2,4  | 2.52 (1.83 to 23.5)                                                      | 3.00 (1.92 to 7.45)                                                      | 3.93 (2.00 to 8.00)                                                      | 3.92 (1.98 to 24.0)                                                       |
| Cycle 1 Day 5 n=6,7,5,0,0,0,0  | 3.44 (1.83 to 4.07)                                                      | 2.90 (2.00 to 3.97)                                                      | 2.87 (1.88 to 3.03)                                                      | 999 (999 to 999)                                                          |
| Cycle 2 Day 1 n=5,6,3,0,0,0,0  | 1.95 (0.980 to 4.10)                                                     | 3.92 (2.83 to 23.9)                                                      | 2.88 (2.08 to 7.07)                                                      | 999 (999 to 999)                                                          |
| Cycle 2 Day 5 n=3,5,3,0,0,0,0  | 3.00 (2.95 to 3.17)                                                      | 2.93 (2.75 to 3.17)                                                      | 3.02 (2.92 to 3.08)                                                      | 999 (999 to 999)                                                          |
| Cycle 1 Day 15 n=0,0,0,9,0,0,0 | 999 (999 to 999)                                                         | 999 (999 to 999)                                                         | 999 (999 to 999)                                                         | 2.50 (0.500 to 4.00)                                                      |
| Cycle 3 Day 1 n=0,0,0,0,5,2,3  | 999 (999 to 999)                                                         | 999 (999 to 999)                                                         | 999 (999 to 999)                                                         | 999 (999 to 999)                                                          |

| End point values | Part 1:<br>Ruxolitinib +<br>Crizanlizumab<br>(Tmax for<br>Crizanlizumab) | Part 1:<br>Ruxolitinib +<br>Sabatolimab<br>(Tmax for<br>Sabatolimab) | Part 1:<br>Ruxolitinib +<br>NIS793 (Tmax<br>for NIS793) |  |
|------------------|--------------------------------------------------------------------------|----------------------------------------------------------------------|---------------------------------------------------------|--|
|------------------|--------------------------------------------------------------------------|----------------------------------------------------------------------|---------------------------------------------------------|--|

| Subject group type             | Subject analysis set | Subject analysis set | Subject analysis set |  |
|--------------------------------|----------------------|----------------------|----------------------|--|
| Number of subjects analysed    | 5                    | 2                    | 4                    |  |
| Units: hours                   |                      |                      |                      |  |
| median (full range (min-max))  |                      |                      |                      |  |
| Cycle 1 Day 1 n=6,9,5,9,5,2,4  | 1.82 (1.50 to 2.27)  | 1.84 (1.67 to 2.00)  | 2.00 (1.95 to 2.98)  |  |
| Cycle 1 Day 5 n=6,7,5,0,0,0,0  | 999 (999 to 999)     | 999 (999 to 999)     | 999 (999 to 999)     |  |
| Cycle 2 Day 1 n=5,6,3,0,0,0,0  | 999 (999 to 999)     | 999 (999 to 999)     | 999 (999 to 999)     |  |
| Cycle 2 Day 5 n=3,5,3,0,0,0,0  | 999 (999 to 999)     | 999 (999 to 999)     | 999 (999 to 999)     |  |
| Cycle 1 Day 15 n=0,0,0,9,0,0,0 | 999 (999 to 999)     | 999 (999 to 999)     | 999 (999 to 999)     |  |
| Cycle 3 Day 1 n=0,0,0,0,5,2,3  | 1.65 (0.750 to 2.13) | 2.01 (1.85 to 2.17)  | 1.97 (1.92 to 2.33)  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Ruxolitinib in Part 1

|                 |                                                                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Time to Reach Maximum (Peak) Plasma, Blood, Serum or Other Body Fluid Drug Concentration After Single Dose Administration (Tmax) for Ruxolitinib in Part 1 <sup>[23]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1 and 5 of Cycles 1 and 2; Day 15 of Cycle 1

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                                   | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|----------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                                 | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed                        | 3                                               | 4                                               | 2                                               | 3                                                |
| Units: hours                                       |                                                 |                                                 |                                                 |                                                  |
| median (full range (min-max))                      |                                                 |                                                 |                                                 |                                                  |
| Ruxolitinib 5 mg Cycle 1 Day 1<br>n=0,0,2,1,0,0,0  | 999 (999 to 999)                                | 999 (999 to 999)                                | 0.960 (0.920 to 1.00)                           | 0.500 (0.500 to 0.500)                           |
| Ruxolitinib 10 mg Cycle 1 Day 1<br>n=3,4,1,2,1,2,1 | 0.550 (0.330 to 6.18)                           | 0.775 (0.500 to 1.08)                           | 0.500 (0.500 to 0.500)                          | 0.485 (0.470 to 0.500)                           |
| Ruxolitinib 15 mg Cycle 1 Day 1<br>n=1,0,2,1,2,0,2 | 0.650 (0.650 to 0.650)                          | 999 (999 to 999)                                | 1.96 (1.92 to 2.00)                             | 0.420 (0.420 to 0.420)                           |
| Ruxolitinib 20 mg Cycle 1 Day 1<br>n=3,2,1,3,1,0,0 | 0.530 (0.500 to 1.00)                           | 1.54 (1.08 to 2.00)                             | 1.00 (1.00 to 1.00)                             | 0.450 (0.420 to 1.03)                            |

|                                                     |                        |                        |                        |                        |
|-----------------------------------------------------|------------------------|------------------------|------------------------|------------------------|
| Ruxolitinib 25 mg Cycle 1 Day 1<br>n=0,0,0,1,0,0,1  | 999 (999 to 999)       | 999 (999 to 999)       | 999 (999 to 999)       | 0.00 (0.00 to 0.00)    |
| Ruxolitinib 5 mg Cycle 1 Day 5<br>n=0,0,2,0,0,0,0   | 999 (999 to 999)       | 999 (999 to 999)       | 0.960 (0.920 to 1.00)  | 999 (999 to 999)       |
| Ruxolitinib 10 mg Cycle 1 Day 5<br>n=3,3,1,0,0,0,0  | 1.00 (0.830 to 2.02)   | 0.980 (0.920 to 2.03)  | 1.00 (1.00 to 1.00)    | 999 (999 to 999)       |
| Ruxolitinib 15 mg Cycle 1 Day 5<br>n=1,1,2,0,0,0,0  | 0.970 (0.970 to 0.970) | 0.830 (0.830 to 0.830) | 0.955 (0.830 to 1.08)  | 999 (999 to 999)       |
| Ruxolitinib 20 mg Cycle 1 Day 5<br>n=2,4,1,0,0,0,0  | 0.925 (0.850 to 1.00)  | 1.00 (0.920 to 1.08)   | 0.830 (0.830 to 0.830) | 999 (999 to 999)       |
| Ruxolitinib 5 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0  | 999 (999 to 999)       | 999 (999 to 999)       | 999 (999 to 999)       | 0.500 (0.500 to 0.500) |
| Ruxolitinib 10 mg Cycle 1 Day 15<br>n=0,0,0,2,0,0,0 | 999 (999 to 999)       | 999 (999 to 999)       | 999 (999 to 999)       | 1.98 (1.95 to 2.00)    |
| Ruxolitinib 15 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (999 to 999)       | 999 (999 to 999)       | 999 (999 to 999)       | 0.500 (0.500 to 0.500) |
| Ruxolitinib 20 mg Cycle 1 Day 15<br>n=0,0,0,3,0,0,0 | 999 (999 to 999)       | 999 (999 to 999)       | 999 (999 to 999)       | 0.650 (0.500 to 1.00)  |
| Ruxolitinib 25 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (999 to 999)       | 999 (999 to 999)       | 999 (999 to 999)       | 0.500 (0.500 to 0.500) |
| Ruxolitinib 5 mg Cycle 2 Day 1<br>n=0,0,1,0,0,0,0   | 999 (999 to 999)       | 999 (999 to 999)       | 0.900 (0.900 to 0.900) | 999 (999 to 999)       |
| Ruxolitinib 10 mg Cycle 2 Day 1<br>n=2,2,1,0,0,0,0  | 0.895 (0.870 to 0.920) | 1.00 (0.920 to 1.08)   | 2.00 (2.00 to 2.00)    | 999 (999 to 999)       |
| Ruxolitinib 15 mg Cycle 2 Day 1<br>n=1,2,2,0,0,0,0  | 1.05 (1.05 to 1.05)    | 1.46 (1.00 to 1.92)    | 4.00 (0.920 to 7.07)   | 999 (999 to 999)       |
| Ruxolitinib 20 mg Cycle 2 Day 1<br>n=3,3,1,0,0,0,0  | 0.980 (0.880 to 1.02)  | 1.02 (1.00 to 4.00)    | 0.930 (0.930 to 0.930) | 999 (999 to 999)       |

| <b>End point values</b>                             | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|-----------------------------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                                  | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed                         | 2                                         | 2                                       | 2                                  |  |
| Units: hours                                        |                                           |                                         |                                    |  |
| median (full range (min-max))                       |                                           |                                         |                                    |  |
| Ruxolitinib 5 mg Cycle 1 Day 1<br>n=0,0,2,1,0,0,0   | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 10 mg Cycle 1 Day 1<br>n=3,4,1,2,1,2,1  | 0.580 (0.580 to 0.580)                    | 0.460 (0.00 to 0.920)                   | 1.67 (1.67 to 1.67)                |  |
| Ruxolitinib 15 mg Cycle 1 Day 1<br>n=1,0,2,1,2,0,2  | 1.80 (1.75 to 1.85)                       | 999 (999 to 999)                        | 2.42 (1.08 to 3.75)                |  |
| Ruxolitinib 20 mg Cycle 1 Day 1<br>n=3,2,1,3,1,0,0  | 1.17 (1.17 to 1.17)                       | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 25 mg Cycle 1 Day 1<br>n=0,0,0,1,0,0,1  | 999 (999 to 999)                          | 999 (999 to 999)                        | 2.00 (2.00 to 2.00)                |  |
| Ruxolitinib 5 mg Cycle 1 Day 5<br>n=0,0,2,0,0,0,0   | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 10 mg Cycle 1 Day 5<br>n=3,3,1,0,0,0,0  | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 15 mg Cycle 1 Day 5<br>n=1,1,2,0,0,0,0  | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 20 mg Cycle 1 Day 5<br>n=2,4,1,0,0,0,0  | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 5 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0  | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |
| Ruxolitinib 10 mg Cycle 1 Day 15<br>n=0,0,0,2,0,0,0 | 999 (999 to 999)                          | 999 (999 to 999)                        | 999 (999 to 999)                   |  |

|                                                     |                  |                  |                  |  |
|-----------------------------------------------------|------------------|------------------|------------------|--|
| Ruxolitinib 15 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |
| Ruxolitinib 20 mg Cycle 1 Day 15<br>n=0,0,0,3,0,0,0 | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |
| Ruxolitinib 25 mg Cycle 1 Day 15<br>n=0,0,0,1,0,0,0 | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |
| Ruxolitinib 5 mg Cycle 2 Day 1<br>n=0,0,1,0,0,0,0   | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |
| Ruxolitinib 10 mg Cycle 2 Day 1<br>n=2,2,1,0,0,0,0  | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |
| Ruxolitinib 15 mg Cycle 2 Day 1<br>n=1,2,2,0,0,0,0  | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |
| Ruxolitinib 20 mg Cycle 2 Day 1<br>n=3,3,1,0,0,0,0  | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration Versus Time Profile for Siremadlin in Part 1

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Concentration Versus Time Profile for Siremadlin in Part 1 <sup>[24]</sup> |
|-----------------|----------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Day 1 of Cycles 1 and 2; Day 6 of Cycle 1; Days 2 and 5 of Cycles 1, 2, 3, 4, 5, and 6. Each cycle was 28 days.

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                       | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg |  |
|----------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                     | Reporting group                                 | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed            | 7                                               | 10                                              | 5                                               |  |
| Units: ng/mL                           |                                                 |                                                 |                                                 |  |
| arithmetic mean (standard deviation)   |                                                 |                                                 |                                                 |  |
| Cycle 1 Day 1, 0 hr (pre-dose) n=6,7,5 | 0 (± 0)                                         | 0 (± 0)                                         | 0 (± 0)                                         |  |
| Cycle 1 Day 1, 0.5 hr n=6,8,5          | 7.46 (± 6.23)                                   | 4.76 (± 8.02)                                   | 12.8 (± 21.0)                                   |  |
| Cycle 1 Day 1, 1 hr n=6,9,5            | 52.7 (± 27.0)                                   | 38.8 (± 40.9)                                   | 87.0 (± 73.6)                                   |  |
| Cycle 1 Day 1, 2 hr n=6,9,5            | 104 (± 53.3)                                    | 146 (± 95.1)                                    | 199 (± 139)                                     |  |
| Cycle 1 Day 1, 3 hr n=6,9,4            | 102 (± 51.8)                                    | 178 (± 96.3)                                    | 192 (± 137)                                     |  |
| Cycle 1 Day 1, 4 hr n=6,9,5            | 92.9 (± 44.0)                                   | 181 (± 116)                                     | 201 (± 109)                                     |  |
| Cycle 1 Day 1, 8 hr n=6,9,5            | 75.7 (± 36.9)                                   | 146 (± 77.0)                                    | 212 (± 55.5)                                    |  |
| Cycle 1 Day 2, 24 hr n=6,10,4          | 42.0 (± 23.7)                                   | 59.7 (± 49.4)                                   | 95.3 (± 41.2)                                   |  |
| Cycle 1 Day 5, 0 hr (pre-dose) n=6,7,5 | 43.5 (± 42.2)                                   | 88.4 (± 73.6)                                   | 77.6 (± 84.2)                                   |  |
| Cycle 1 Day 5, 1 hr n=6,6,5            | 72.9 (± 28.3)                                   | 171 (± 89.8)                                    | 155 (± 123)                                     |  |
| Cycle 1 Day 5, 2 hr n=6,7,5            | 127 (± 63.7)                                    | 260 (± 128)                                     | 324 (± 112)                                     |  |
| Cycle 1 Day 5, 3 hr n=6,7,5            | 144 (± 74.6)                                    | 260 (± 130)                                     | 333 (± 108)                                     |  |

|                                        |               |               |               |
|----------------------------------------|---------------|---------------|---------------|
| Cycle 1 Day 5, 4 hr n=5,7,5            | 133 (± 67.4)  | 226 (± 111)   | 295 (± 97.9)  |
| Cycle 1 Day 5, 8 hr n=7,8,3            | 110 (± 54.3)  | 160 (± 83.1)  | 247 (± 126)   |
| Cycle 1 Day 6, 24 hr n=7,8,5           | 45.4 (± 35.9) | 75.1 (± 66.5) | 72.2 (± 90.5) |
| Cycle 2 Day 1, 0 hr (pre-dose) n=4,5,3 | 0 (± 0)       | 0 (± 0)       | 0 (± 0)       |
| Cycle 2 Day 1, 1 hr n=5,5,3            | 71.8 (± 92.9) | 25.5 (± 28.4) | 32.2 (± 28.7) |
| Cycle 2 Day 1, 2 hr n=5,5,2            | 116 (± 64.7)  | 100 (± 64.8)  | 144 (± 200)   |
| Cycle 2 Day 1, 3 hr n=5,5,3            | 111 (± 58.2)  | 146 (± 99.5)  | 178 (± 147)   |
| Cycle 2 Day 1, 4 hr n=5,5,3            | 114 (± 52.8)  | 158 (± 78.4)  | 164 (± 102)   |
| Cycle 2 Day 1, 8 hr n=4,5,3            | 90.9 (± 39.1) | 122 (± 54.5)  | 189 (± 63.2)  |
| Cycle 2 Day 2, 24 hr n=4,5,3           | 67.3 (± 49.3) | 48.5 (± 44.2) | 31.7 (± 5.42) |
| Cycle 2 Day 5, 0 hr (pre-dose) n=4,7,3 | 24.3 (± 23.8) | 42.5 (± 50.8) | 29.2 (± 6.67) |
| Cycle 2 Day 5, 3 hr n=3,6,3            | 103 (± 34.1)  | 181 (± 89.7)  | 228 (± 58.3)  |
| Cycle 2 Day 6, 24 hr n=4,5,3           | 34.7 (± 13.2) | 51.5 (± 58.3) | 27.5 (± 6.45) |
| Cycle 3 Day 2, 0 hr (pre-dose) n=3,4,4 | 43.5 (± 16.5) | 79.1 (± 96.9) | 39.2 (± 20.5) |
| Cycle 3 Day 5, 0 hr (pre-dose) n=5,6,3 | 56.8 (± 47.9) | 81.0 (± 73.9) | 29.7 (± 23.3) |
| Cycle 4 Day 2, 0 hr (pre-dose) n=5,5,1 | 36.3 (± 21.7) | 63.0 (± 52.4) | 10.9 (± 999)  |
| Cycle 4 Day 5, 0 hr (pre-dose) n=5,6,1 | 40.4 (± 29.7) | 50.1 (± 48.1) | 10.5 (± 999)  |
| Cycle 5 Day 2, 0 hr (pre-dose) n=6,4,4 | 40.0 (± 29.3) | 146 (± 180)   | 49.2 (± 25.1) |
| Cycle 5 Day 5, 0 hr (pre-dose) n=6,4,3 | 78.3 (± 90.2) | 124 (± 129)   | 32.5 (± 13.5) |
| Cycle 6 Day 2, 0 hr (pre-dose) n=5,2,1 | 48.0 (± 28.2) | 60.2 (± 37.0) | 16.4 (± 999)  |
| Cycle 6 Day 5, 0 hr (pre-dose) n=4,2,1 | 79.0 (± 52.2) | 68.9 (± 68.1) | 9.02 (± 999)  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration Versus Time Profile for Rineterkib in Part 1

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Concentration Versus Time Profile for Rineterkib in Part 1 <sup>[25]</sup> |
|-----------------|----------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1, 2, 15, and 16 of Cycle 1; Day 1 of Cycles 2, 3, 4, 5, and 6. Each cycle was 28 days.

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                     | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |  |  |  |
|--------------------------------------|--------------------------------------------------|--|--|--|
| Subject group type                   | Reporting group                                  |  |  |  |
| Number of subjects analysed          | 9                                                |  |  |  |
| Units: ng/mL                         |                                                  |  |  |  |
| arithmetic mean (standard deviation) |                                                  |  |  |  |
| Cycle 1 Day 1, 0 hr (pre-dose) n=9   | 0 (± 0)                                          |  |  |  |
| Cycle 1 Day 1, 0.5 hr n=9            | 68.3 (± 68.8)                                    |  |  |  |
| Cycle 1 Day 1, 1 hr n=8              | 235 (± 343)                                      |  |  |  |

|                                     |             |  |  |  |
|-------------------------------------|-------------|--|--|--|
| Cycle 1 Day 1, 2 hr n=8             | 340 (± 229) |  |  |  |
| Cycle 1 Day 1, 3 hr n=9             | 352 (± 244) |  |  |  |
| Cycle 1 Day 1, 4 hr n=9             | 325 (± 173) |  |  |  |
| Cycle 1 Day 1, 8 hr n=7             | 244 (± 128) |  |  |  |
| Cycle 1 Day 2, 24 hr n=9            | 261 (± 419) |  |  |  |
| Cycle 1 Day 2, 0 hr (pre-dose) n=8  | 234 (± 440) |  |  |  |
| Cycle 1 Day 15, 0 hr (pre-dose) n=8 | 330 (± 222) |  |  |  |
| Cycle 1 Day 15 0.5 hr n=8           | 581 (± 464) |  |  |  |
| Cycle 1 Day 15, 1 hr n=n=9          | 735 (± 620) |  |  |  |
| Cycle 1 Day 15, 2 hr n=8            | 749 (± 512) |  |  |  |
| Cycle 1 Day 15, 3 hr n=8            | 789 (± 616) |  |  |  |
| Cycle 1 Day 15, 4 hr n=8            | 771 (± 484) |  |  |  |
| Cycle 1 Day 15, 8 hr n=9            | 633 (± 403) |  |  |  |
| Cycle 1 Day 16, 24 hr n=8           | 528 (± 618) |  |  |  |
| Cycle 1 Day 16, 0 hr (pre-dose) n=8 | 305 (± 222) |  |  |  |
| Cycle 2 Day 1, 0 hr (pre-dose) n=9  | 314 (± 171) |  |  |  |
| Cycle 3 Day 1, 0 hr (pre-dose) n=6  | 406 (± 341) |  |  |  |
| Cycle 4 Day 1, 0 hr (pre-dose) n=5  | 402 (± 364) |  |  |  |
| Cycle 5 Day 1, 0 hr (pre-dose) n=3  | 232 (± 165) |  |  |  |
| Cycle 6 Day 1, 0 hr (pre-dose) n=3  | 340 (± 125) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration Versus Time Profile for Crizanlizumab in Part 1

|                 |                                                             |
|-----------------|-------------------------------------------------------------|
| End point title | Concentration Versus Time Profile for Crizanlizumab in Part |
|-----------------|-------------------------------------------------------------|

End point description:

EOI = end of infusion

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

End point timeframe:

Days 1, 2, 8, and 15 of Cycles 1, 2, and 3; Day 1 of Cycles 4, 5, 6, and 9. Each cycle was 28 days.

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

|                                                  |                                           |  |  |  |
|--------------------------------------------------|-------------------------------------------|--|--|--|
| <b>End point values</b>                          | Part 1:<br>Ruxolitinib +<br>Crizanlizumab |  |  |  |
| Subject group type                               | Reporting group                           |  |  |  |
| Number of subjects analysed                      | 5                                         |  |  |  |
| Units: ng/mL                                     |                                           |  |  |  |
| arithmetic mean (standard deviation)             |                                           |  |  |  |
| Cycle 1 Day 1, 0 H / PRE-INFUSION n=4            | 0 (± 0)                                   |  |  |  |
| Cycle 1 Day 1, 1H POST EOI n=5                   | 114000 (±<br>36400)                       |  |  |  |
| Cycle 1 Day 2, 24H POST START OF<br>INFUSION n=4 | 78700 (±<br>10500)                        |  |  |  |

|                                                 |                  |  |  |  |
|-------------------------------------------------|------------------|--|--|--|
| Cycle 1 Day 8, 168H POST START OF INFUSION n=5  | 28700 (± 12200)  |  |  |  |
| Cycle 1 Day 15, 336H POST START OF INFUSION n=5 | 9280 (± 4540)    |  |  |  |
| Cycle 1 Day 15, 0 H / PRE-INFUSION n=1          | 7710 (± 999)     |  |  |  |
| Cycle 2 Day 1, 0 H / PRE-INFUSION n=5           | 20700 (± 8980)   |  |  |  |
| Cycle 2 Day 1, 1H POST EOI n=5                  | 135000 (± 43100) |  |  |  |
| Cycle 2 Day 1, 336H POST START OF INFUSION n=1, | 15500 (± 999)    |  |  |  |
| Cycle 3 Day 1, 672H POST START OF INFUSION n=5  | 8710 (± 8350)    |  |  |  |
| Cycle 3 Day 1, 0 H / PRE-INFUSION n=5           | 8710 (± 8350)    |  |  |  |
| Cycle 3 Day 1, 1H POST EOI n=4                  | 103000 (± 59200) |  |  |  |
| Cycle 3 Day 2, 24H POST START OF INFUSION n=5   | 95500 (± 42300)  |  |  |  |
| Cycle 3 Day 8, 168H POST START OF INFUSION n=5  | 37100 (± 19400)  |  |  |  |
| Cycle 3 Day 15, 336H POST START OF INFUSION n=5 | 21000 (± 17700)  |  |  |  |
| Cycle 4 Day 1, 672H POST START OF INFUSION n=5  | 5900 (± 6710)    |  |  |  |
| Cycle 4 Day 1, 0 H / PRE-INFUSION n=5           | 5900 (± 6710)    |  |  |  |
| Cycle 4 Day 1, 1H POST EOI n=5                  | 128000 (± 33200) |  |  |  |
| Cycle 5 Day 1, 672H POST START OF INFUSION n=4  | 6780 (± 7830)    |  |  |  |
| Cycle 5 Day 1, 0 H / PRE-INFUSION n=4           | 6780 (± 7830)    |  |  |  |
| Cycle 5 Day 1, 1H POST EOI n=3                  | 122000 (± 29400) |  |  |  |
| Cycle 6 Day 1, 672H POST START OF INFUSION n=4  | 6930 (± 8000)    |  |  |  |
| Cycle 6 Day 1, 0 H / PRE-INFUSION n=4           | 6930 (± 8000)    |  |  |  |
| Cycle 6 Day 1, 1H POST EOI n=4                  | 128000 (± 39600) |  |  |  |
| Cycle 9 Day 1, 0 H / PRE-INFUSION n=3           | 5500 (± 9530)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration Versus Time Profile for Sabatolimab in Part 1

|                 |                                                                             |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Concentration Versus Time Profile for Sabatolimab in Part 1 <sup>[27]</sup> |
|-----------------|-----------------------------------------------------------------------------|

End point description:

EOI = end of infusion

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

End point timeframe:

Days 1, 2, 8, and 15 of Cycles 1, 2, and 3; Day 1 of Cycles 4 and 5. Each cycle was 28 days.

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.



| End point values                                   | Part 1:<br>Ruxolitinib +<br>Sabatolimab |  |  |  |
|----------------------------------------------------|-----------------------------------------|--|--|--|
| Subject group type                                 | Reporting group                         |  |  |  |
| Number of subjects analysed                        | 2                                       |  |  |  |
| Units: ng/mL                                       |                                         |  |  |  |
| arithmetic mean (standard deviation)               |                                         |  |  |  |
| Cycle 1 Day 1, 0 H / PRE-INFUSION n=2              | 0 (± 0)                                 |  |  |  |
| Cycle 1 Day 1, 1H POST EOI n=1                     | 143 (± 999)                             |  |  |  |
| Cycle 1 Day 2, 24H POST START OF<br>INFUSION n=2   | 109 (± 13.2)                            |  |  |  |
| Cycle 1 Day 8, 168H POST START OF<br>INFUSION n=1  | 57.0 (± 999)                            |  |  |  |
| Cycle 1 Day 15, 336H POST START OF<br>INFUSION n=2 | 41.8 (± 7.28)                           |  |  |  |
| Cycle 2 Day 1, 672H POST START OF<br>INFUSION n=2  | 16.1 (± 9.16)                           |  |  |  |
| Cycle 2 Day 1, 0 H / PRE-INFUSION n=2              | 16.1 (± 9.16)                           |  |  |  |
| Cycle 2 Day 1, 1H POST EOI n=1                     | 126 (± 999)                             |  |  |  |
| Cycle 3 Day 1, 672H POST START OF<br>INFUSION n=2  | 26.0 (± 5.09)                           |  |  |  |
| Cycle 3 Day 1, 0 H / PRE-INFUSION n=2              | 26.0 (± 5.09)                           |  |  |  |
| Cycle 3 Day 1, 1H POST EOI n=2                     | 150 (± 33.2)                            |  |  |  |
| Cycle 3 Day 2, 24H POST START OF<br>INFUSION n=2   | 125 (± 10.6)                            |  |  |  |
| Cycle 3 Day 8, 168H POST START OF<br>INFUSION n=2  | 80.5 (± 19.1)                           |  |  |  |
| Cycle 3 Day 15, 336H POST START OF<br>INFUSION n=2 | 58.0 (± 12.3)                           |  |  |  |
| Cycle 4 Day 1, 672H POST START OF<br>INFUSION n=1  | 31.1 (± 999)                            |  |  |  |
| Cycle 4 Day 1, 0 H / PRE-INFUSION n=2              | 30.0 (± 1.56)                           |  |  |  |
| Cycle 4 Day 1, 1H POST EOI n=2                     | 141 (± 11.3)                            |  |  |  |
| Cycle 5 Day 1, 0 H / PRE-INFUSION n=2              | 32.9 (± 3.82)                           |  |  |  |
| Cycle 5 Day 1, 1H POST EOI n=2                     | 152 (± 9.19)                            |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration Versus Time Profile for NIS793 in Part 1

|                 |                                                                        |
|-----------------|------------------------------------------------------------------------|
| End point title | Concentration Versus Time Profile for NIS793 in Part 1 <sup>[28]</sup> |
|-----------------|------------------------------------------------------------------------|

End point description:

EOI = end of infusion

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

End point timeframe:

Days 1, 2, 4, 8, 11, and 15 of Cycles 1, 2, and 3; Day 1 of Cycles 4 and 5. Each cycle was 28 days.

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                                | Part 1:<br>Ruxolitinib +<br>NIS793 |  |  |  |
|-------------------------------------------------|------------------------------------|--|--|--|
| Subject group type                              | Reporting group                    |  |  |  |
| Number of subjects analysed                     | 4                                  |  |  |  |
| Units: ng/mL                                    |                                    |  |  |  |
| arithmetic mean (standard deviation)            |                                    |  |  |  |
| Cycle 1 Day 1, 0 H / PRE-INFUSION n=4           | 0 (± 0)                            |  |  |  |
| Cycle 1 Day 1, 1H POST EOI n=4                  | 439000 (± 56100)                   |  |  |  |
| Cycle 1 Day 2, 24H POST START OF INFUSION n=4   | 349000 (± 52800)                   |  |  |  |
| Cycle 1 Day 4, 72H POST START OF INFUSION n=4   | 279000 (± 48400)                   |  |  |  |
| Cycle 1 Day 8, 168H POST START OF INFUSION n=3  | 196000 (± 31000)                   |  |  |  |
| Cycle 1 Day 11, 240H POST START OF INFUSION n=4 | 183000 (± 45400)                   |  |  |  |
| Cycle 1 Day 15, 336H POST START OF INFUSION n=4 | 161000 (± 37500)                   |  |  |  |
| Cycle 2 Day 1, 504H POST START OF INFUSION n=4  | 132000 (± 33300)                   |  |  |  |
| Cycle 2 Day 1, 0 H / PRE-INFUSION n=4           | 132000 (± 33300)                   |  |  |  |
| Cycle 3 Day 1, 0 H / PRE-INFUSION n=3           | 187000 (± 61000)                   |  |  |  |
| Cycle 3 Day 1, 1H POST EOI n=3                  | 743000 (± 314000)                  |  |  |  |
| Cycle 3 Day 2, 24H POST START OF INFUSION n=2   | 632000 (± 17000)                   |  |  |  |
| Cycle 3 Day 4, 72H POST START OF INFUSION n=3   | 448000 (± 114000)                  |  |  |  |
| Cycle 3 Day 8, 168H POST START OF INFUSION n=3  | 383000 (± 103000)                  |  |  |  |
| Cycle 3 Day 11, 240H POST START OF INFUSION n=2 | 262000 (± 93300)                   |  |  |  |
| Cycle 3 Day 15, 336H POST START OF INFUSION n=3 | 265000 (± 51500)                   |  |  |  |
| Cycle 4 Day 1, 504H POST START OF INFUSION n=1  | 281000 (± 999)                     |  |  |  |
| Cycle 4 Day 1, 0 H / PRE-INFUSION n=2           | 232000 (± 70000)                   |  |  |  |
| Cycle 5 Day 1, 0 H / PRE-INFUSION n=1           | 280000 (± 999)                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration Versus Time Profile for Ruxolitinib in Part 1

|                 |                                                                             |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Concentration Versus Time Profile for Ruxolitinib in Part 1 <sup>[29]</sup> |
|-----------------|-----------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Days 1, 2, 5, 6, and 15 of Cycles 1 and 2; Day 16 of Cycle 1; Days 1, 2, and 15 of Cycle 3; Days 1 and 5 of Cycles 4, 5, and 6. Each cycle was 28 days.

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Applicable to Part 1 only.

| End point values                                   | Part 1:<br>Ruxolitinib +<br>Siremadlin 20<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 30<br>mg | Part 1:<br>Ruxolitinib +<br>Siremadlin 40<br>mg | Part 1:<br>Ruxolitinib +<br>Rineterkib 200<br>mg |
|----------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------------------|
| Subject group type                                 | Reporting group                                 | Reporting group                                 | Reporting group                                 | Reporting group                                  |
| Number of subjects analysed                        | 7                                               | 8                                               | 6                                               | 8                                                |
| Units: ng/mL                                       |                                                 |                                                 |                                                 |                                                  |
| arithmetic mean (standard deviation)               |                                                 |                                                 |                                                 |                                                  |
| Cycle 1 Day 1, 0 hr (pre-dose)<br>n=6,6,5,7,3,2,4  | 34.7 (± 17.8)                                   | 21.3 (± 14.5)                                   | 11.8 (± 13.4)                                   | 20.1 (± 16.1)                                    |
| Cycle 1 Day 1, 0.5 hr n=6,5,6,8,2,2,3              | 284 (± 128)                                     | 152 (± 91.1)                                    | 95.7 (± 63.2)                                   | 185 (± 100)                                      |
| Cycle 1 Day 1, 1 hr n=6,6,6,7,2,2,3                | 240 (± 78.9)                                    | 167 (± 51.7)                                    | 124 (± 64.5)                                    | 192 (± 106)                                      |
| Cycle 1 Day 1, 2 hr n=6,6,6,7,2,2,3                | 174 (± 55.3)                                    | 143 (± 48.6)                                    | 98.9 (± 46.2)                                   | 140 (± 112)                                      |
| Cycle 1 Day 1, 3 hr n=6,6,5,8,2,2,3                | 125 (± 36.6)                                    | 114 (± 42.1)                                    | 62.4 (± 31.1)                                   | 97.4 (± 75.7)                                    |
| Cycle 1 Day 1, 4 hr n=6,6,6,8,2,2,3                | 93.2 (± 26.5)                                   | 77.8 (± 40.0)                                   | 50.2 (± 23.4)                                   | 59.2 (± 46.1)                                    |
| Cycle 1 Day 1, 8 hr n=6,6,6,8,4,2,3                | 51.6 (± 18.7)                                   | 32.2 (± 19.1)                                   | 24.0 (± 15.0)                                   | 29.9 (± 19.8)                                    |
| Cycle 1 Day 2, 0 hr (pre-dose)<br>n=7,6,4,8,1,1,0  | 18.2 (± 13.0)                                   | 13.4 (± 11.1)                                   | 11.2 (± 16.2)                                   | 17.6 (± 19.9)                                    |
| Cycle 1 Day 5, 0 hr (pre-dose)<br>n=6,8,6,0,0,0,0  | 15.5 (± 13.9)                                   | 14.7 (± 14.0)                                   | 9.33 (± 10.6)                                   | 999 (± 999)                                      |
| Cycle 1 Day 5, 1 hr n=6,7,6,0,0,0,0                | 160 (± 79.5)                                    | 221 (± 83.7)                                    | 130 (± 66.6)                                    | 999 (± 999)                                      |
| Cycle 1 Day 5, 2 hr n=6,8,6,0,0,0,0                | 149 (± 64.0)                                    | 140 (± 45.6)                                    | 90.0 (± 41.4)                                   | 999 (± 999)                                      |
| Cycle 1 Day 5, 3 hr n=6,8,6,0,0,0,0                | 104 (± 45.2)                                    | 100 (± 39.1)                                    | 61.8 (± 31.7)                                   | 999 (± 999)                                      |
| Cycle 1 Day 5, 4 hr n=6,8,6,0,0,0,0                | 81.4 (± 38.4)                                   | 71.2 (± 30.1)                                   | 34.1 (± 16.1)                                   | 999 (± 999)                                      |
| Cycle 1 Day 5, 8 hr n=6,8,4,0,0,0,0                | 37.6 (± 22.6)                                   | 22.9 (± 13.7)                                   | 16.2 (± 13.4)                                   | 999 (± 999)                                      |
| Cycle 1 Day 6, 0 hr (pre-dose)<br>n=6,7,5,0,0,0,0  | 11.5 (± 12.1)                                   | 37.8 (± 63.4)                                   | 6.28 (± 9.31)                                   | 999 (± 999)                                      |
| Cycle 1 Day 15, 0 hr (pre-dose)<br>n=7,8,4,7,3,2,0 | 23.2 (± 34.0)                                   | 23.6 (± 19.8)                                   | 11.2 (± 17.4)                                   | 11.9 (± 14.2)                                    |
| Cycle 1 Day 15, 0.5 hr n=0,0,0,7,0,0,0             | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 231 (± 115)                                      |
| Cycle 1 Day 15, 1 hr n=0,0,0,8,0,0,0               | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 194 (± 139)                                      |
| Cycle 1 Day 15, 2 hr n=0,0,0,7,0,0,0               | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 126 (± 58.7)                                     |
| Cycle 1 Day 15, 3 hr n=0,0,0,7,0,0,0               | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 103 (± 59.6)                                     |
| Cycle 1 Day 15, 4 hr n=0,0,0,7,0,0,0               | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 76.3 (± 53.5)                                    |
| Cycle 1 Day 15, 8 hr n=0,0,0,8,0,0,0               | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 27.9 (± 21.7)                                    |
| Cycle 1 Day 16, 0 hr (pre-dose)<br>n=0,0,0,6,0,0,0 | 999 (± 999)                                     | 999 (± 999)                                     | 999 (± 999)                                     | 14.4 (± 15.2)                                    |
| Cycle 2 Day 1, 0 hr (pre-dose)<br>n=6,7,5,8,4,2,3  | 25.9 (± 23.4)                                   | 19.3 (± 18.8)                                   | 11.4 (± 20.7)                                   | 45.7 (± 108)                                     |
| Cycle 2 Day 1, 1 hr n=6,7,5,0,0,0,0                | 212 (± 89.8)                                    | 186 (± 113)                                     | 114 (± 82.4)                                    | 999 (± 999)                                      |
| Cycle 2 Day 1, 2 hr n=6,7,4,0,0,0,0                | 144 (± 76.0)                                    | 165 (± 82.2)                                    | 56.2 (± 30.9)                                   | 999 (± 999)                                      |
| Cycle 2 Day 1, 3 hr n=6,7,5,0,0,0,0                | 108 (± 50.8)                                    | 127 (± 61.7)                                    | 50.3 (± 26.4)                                   | 999 (± 999)                                      |

|                                                    |               |               |                  |               |
|----------------------------------------------------|---------------|---------------|------------------|---------------|
| Cycle 2 Day 1, 4 hr n=5,7,5,0,0,0,0                | 89.9 (± 39.8) | 106 (± 39.5)  | 45.6 (± 25.8)    | 999 (± 999)   |
| Cycle 2 Day 1, 8 hr n=4,6,5,0,0,0,0                | 47.3 (± 31.5) | 45.8 (± 19.4) | 30.9 (± 28.1)    | 999 (± 999)   |
| Cycle 2 Day 2, 0 hr (pre-dose)<br>n=3,6,5,0,0,0,0  | 74.0 (± 62.3) | 19.2 (± 19.7) | 13.9 (± 20.5)    | 999 (± 999)   |
| Cycle 2 Day 5, 0 hr (pre-dose)<br>n=3,8,4,0,0,0,0  | 15.4 (± 6.29) | 15.2 (± 11.3) | 4.45 (± 4.57)    | 999 (± 999)   |
| Cycle 2 Day 6, 0 hr (pre-dose)<br>n=4,5,4,0,0,0,0  | 7.36 (± 7.32) | 46.8 (± 80.0) | 2.40 (± 2.74)    | 999 (± 999)   |
| Cycle 2 Day 15, 0 hr (pre-dose)<br>n=6,8,3,0,1,2,0 | 22.4 (± 17.2) | 22.1 (± 22.7) | 1.93 (± 1.65)    | 999 (± 999)   |
| Cycle 3 Day 1, 0 hr (pre-dose)<br>n=7,7,4,6,4,2,2  | 24.2 (± 15.5) | 23.2 (± 21.8) | 4.50 (± 4.03)    | 11.1 (± 10.9) |
| Cycle 3 Day 2, 0 hr (pre-dose)<br>n=5,6,3,0,0,0,0  | 12.6 (± 13.9) | 31.9 (± 38.9) | 2.33 (± 1.57)    | 999 (± 999)   |
| Cycle 3 Day 15, 0 hr (pre-dose)<br>n=5,5,2,0,4,2,0 | 18.7 (± 18.4) | 45.2 (± 41.5) | 3.95 (± 4.10)    | 999 (± 999)   |
| Cycle 4 Day 1, 0 hr (pre-dose)<br>n=7,5,3,5,4,1,1  | 17.5 (± 18.2) | 20.9 (± 22.2) | 4.53 (± 6.44)    | 18.2 (± 33.8) |
| Cycle 4 Day 5, 0 hr (pre-dose)<br>n=5,6,3,0,0,0,0  | 13.6 (± 13.7) | 9.12 (± 13.5) | 7.99 (± 11.4)    | 999 (± 999)   |
| Cycle 5 Day 1, 0 hr (pre-dose)<br>n=7,6,4,3,3,0,0  | 16.4 (± 16.1) | 12.7 (± 12.0) | 5.30 (± 5.94)    | 10.3 (± 13.6) |
| Cycle 5 Day 5, 0 hr (pre-dose)<br>n=5,3,3,0,0,0,0  | 26.6 (± 16.4) | 9.54 (± 13.2) | 2.79 (± 2.46)    | 999 (± 999)   |
| Cycle 6 Day 1, 0 hr (pre-dose)<br>n=4,4,2,3,3,0,0  | 15.8 (± 19.5) | 17.0 (± 19.7) | 0.608 (± 0.0672) | 21.9 (± 23.2) |
| Cycle 6 Day 5, 0 hr (pre-dose)<br>n=3,4,2,0,0,0,0  | 24.8 (± 19.9) | 11.5 (± 8.34) | 0.957 (± 0.528)  | 999 (± 999)   |

| End point values                                  | Part 1:<br>Ruxolitinib +<br>Crizanlizumab | Part 1:<br>Ruxolitinib +<br>Sabatolimab | Part 1:<br>Ruxolitinib +<br>NIS793 |  |
|---------------------------------------------------|-------------------------------------------|-----------------------------------------|------------------------------------|--|
| Subject group type                                | Reporting group                           | Reporting group                         | Reporting group                    |  |
| Number of subjects analysed                       | 4                                         | 2                                       | 4                                  |  |
| Units: ng/mL                                      |                                           |                                         |                                    |  |
| arithmetic mean (standard deviation)              |                                           |                                         |                                    |  |
| Cycle 1 Day 1, 0 hr (pre-dose)<br>n=6,6,5,7,3,2,4 | 12.9 (± 6.31)                             | 51.2 (± 61.0)                           | 37.9 (± 48.4)                      |  |
| Cycle 1 Day 1, 0.5 hr n=6,5,6,8,2,2,3             | 107 (± 119)                               | 57.1 (± 44.0)                           | 108 (± 128)                        |  |
| Cycle 1 Day 1, 1 hr n=6,6,6,7,2,2,3               | 65.7 (± 59.9)                             | 110 (± 44.1)                            | 164 (± 140)                        |  |
| Cycle 1 Day 1, 2 hr n=6,6,6,7,2,2,3               | 170 (± 140)                               | 72.7 (± 4.10)                           | 187 (± 105)                        |  |
| Cycle 1 Day 1, 3 hr n=6,6,5,8,2,2,3               | 124 (± 91.0)                              | 54.4 (± 10.4)                           | 184 (± 77.9)                       |  |
| Cycle 1 Day 1, 4 hr n=6,6,6,8,2,2,3               | 101 (± 81.2)                              | 28.3 (± 7.28)                           | 190 (± 58.4)                       |  |
| Cycle 1 Day 1, 8 hr n=6,6,6,8,4,2,3               | 39.5 (± 29.2)                             | 7.75 (± 1.52)                           | 44.4 (± 35.3)                      |  |
| Cycle 1 Day 2, 0 hr (pre-dose)<br>n=7,6,4,8,1,1,0 | 30.3 (± 999)                              | 0 (± 999)                               | 999 (± 999)                        |  |
| Cycle 1 Day 5, 0 hr (pre-dose)<br>n=6,8,6,0,0,0,0 | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Cycle 1 Day 5, 1 hr n=6,7,6,0,0,0,0               | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Cycle 1 Day 5, 2 hr n=6,8,6,0,0,0,0               | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Cycle 1 Day 5, 3 hr n=6,8,6,0,0,0,0               | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Cycle 1 Day 5, 4 hr n=6,8,6,0,0,0,0               | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Cycle 1 Day 5, 8 hr n=6,8,4,0,0,0,0               | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |
| Cycle 1 Day 6, 0 hr (pre-dose)<br>n=6,7,5,0,0,0,0 | 999 (± 999)                               | 999 (± 999)                             | 999 (± 999)                        |  |

|                                                    |               |               |               |
|----------------------------------------------------|---------------|---------------|---------------|
| Cycle 1 Day 15, 0 hr (pre-dose)<br>n=7,8,4,7,3,2,0 | 12.6 (± 10.1) | 4.06 (± 2.28) | 999 (± 999)   |
| Cycle 1 Day 15, 0.5 hr n=0,0,0,7,0,0,0             | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 1 Day 15, 1 hr n=0,0,0,8,0,0,0               | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 1 Day 15, 2 hr n=0,0,0,7,0,0,0               | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 1 Day 15, 3 hr n=0,0,0,7,0,0,0               | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 1 Day 15, 4 hr n=0,0,0,7,0,0,0               | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 1 Day 15, 8 hr n=0,0,0,8,0,0,0               | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 1 Day 16, 0 hr (pre-dose)<br>n=0,0,0,6,0,0,0 | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 1, 0 hr (pre-dose)<br>n=6,7,5,8,4,2,3  | 13.7 (± 4.84) | 28.4 (± 39.1) | 65.1 (± 88.9) |
| Cycle 2 Day 1, 1 hr n=6,7,5,0,0,0,0                | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 1, 2 hr n=6,7,4,0,0,0,0                | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 1, 3 hr n=6,7,5,0,0,0,0                | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 1, 4 hr n=5,7,5,0,0,0,0                | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 1, 8 hr n=4,6,5,0,0,0,0                | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 2, 0 hr (pre-dose)<br>n=3,6,5,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 5, 0 hr (pre-dose)<br>n=3,8,4,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 6, 0 hr (pre-dose)<br>n=4,5,4,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 2 Day 15, 0 hr (pre-dose)<br>n=6,8,3,0,1,2,0 | 63.6 (± 999)  | 7.95 (± 8.14) | 999 (± 999)   |
| Cycle 3 Day 1, 0 hr (pre-dose)<br>n=7,7,4,6,4,2,2  | 12.0 (± 6.36) | 2.44 (± 1.46) | 84.6 (± 96.8) |
| Cycle 3 Day 2, 0 hr (pre-dose)<br>n=5,6,3,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 3 Day 15, 0 hr (pre-dose)<br>n=5,5,2,0,4,2,0 | 10.9 (± 6.89) | 12.5 (± 9.14) | 999 (± 999)   |
| Cycle 4 Day 1, 0 hr (pre-dose)<br>n=7,5,3,5,4,1,1  | 14.0 (± 7.81) | 2.94 (± 999)  | 24.4 (± 999)  |
| Cycle 4 Day 5, 0 hr (pre-dose)<br>n=5,6,3,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 5 Day 1, 0 hr (pre-dose)<br>n=7,6,4,3,3,0,0  | 20.1 (± 23.0) | 999 (± 999)   | 999 (± 999)   |
| Cycle 5 Day 5, 0 hr (pre-dose)<br>n=5,3,3,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |
| Cycle 6 Day 1, 0 hr (pre-dose)<br>n=4,4,2,3,3,0,0  | 27.3 (± 32.8) | 999 (± 999)   | 999 (± 999)   |
| Cycle 6 Day 5, 0 hr (pre-dose)<br>n=3,4,2,0,0,0,0  | 999 (± 999)   | 999 (± 999)   | 999 (± 999)   |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus post-treatment safety follow-up, up to a maximum duration of approximately 44 months.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 27.0   |

### Reporting groups

|                       |                                        |
|-----------------------|----------------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Siremadlin 20 mg |
|-----------------------|----------------------------------------|

Reporting group description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                       |                                        |
|-----------------------|----------------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Siremadlin 40 mg |
|-----------------------|----------------------------------------|

Reporting group description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Siremadlin |
|-----------------------|----------------------------------|

Reporting group description:

Total

|                       |                                        |
|-----------------------|----------------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Siremadlin 30 mg |
|-----------------------|----------------------------------------|

Reporting group description:

Dose escalation of siremadlin added to existing stable dose of ruxolitinib

|                       |                                         |
|-----------------------|-----------------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Rineterkib 200 mg |
|-----------------------|-----------------------------------------|

Reporting group description:

Dose escalation of rineterkib added to existing stable dose of ruxolitinib

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Part 1: Ruxolitinib + NIS793 |
|-----------------------|------------------------------|

Reporting group description:

Safety run-in of NIS793 added to existing stable dose of ruxolitinib

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Crizanlizumab |
|-----------------------|-------------------------------------|

Reporting group description:

Safety run-in of crizanlizumab added to existing stable dose of ruxolitinib

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Part 1: Ruxolitinib + Sabatolimab |
|-----------------------|-----------------------------------|

Reporting group description:

Safety run-in of sabatolimab added to existing stable dose of ruxolitinib

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Part 2: Ruxolitinib |
|-----------------------|---------------------|

Reporting group description:

Existing stable dose of ruxolitinib as control for Part 2

|                       |              |
|-----------------------|--------------|
| Reporting group title | All Subjects |
|-----------------------|--------------|

Reporting group description:

All Subjects

| Serious adverse events                            | Part 1: Ruxolitinib + Siremadlin 20 mg | Part 1: Ruxolitinib + Siremadlin 40 mg | Part 1: Ruxolitinib + Siremadlin |
|---------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------|
| Total subjects affected by serious adverse events |                                        |                                        |                                  |
| subjects affected / exposed                       | 2 / 7 (28.57%)                         | 4 / 6 (66.67%)                         | 9 / 23 (39.13%)                  |
| number of deaths (all causes)                     | 0                                      | 3                                      | 3                                |
| number of deaths resulting from                   | 0                                      | 1                                      | 1                                |

|                                                                     |                |                |                |
|---------------------------------------------------------------------|----------------|----------------|----------------|
| adverse events                                                      |                |                |                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Prostate cancer                                                     |                |                |                |
| subjects affected / exposed                                         | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                                                  |                |                |                |
| Aortic aneurysm rupture                                             |                |                |                |
| subjects affected / exposed                                         | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (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          |
| Haemorrhage                                                         |                |                |                |
| subjects affected / exposed                                         | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 1 / 1          | 1 / 1          |
| General disorders and administration site conditions                |                |                |                |
| Multiple organ dysfunction syndrome                                 |                |                |                |
| subjects affected / exposed                                         | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 1          | 0 / 1          |
| Pyrexia                                                             |                |                |                |
| subjects affected / exposed                                         | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders                            |                |                |                |
| Uterine prolapse                                                    |                |                |                |
| subjects affected / exposed                                         | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders                     |                |                |                |
| Acute respiratory failure                                           |                |                |                |
| subjects affected / exposed                                         | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (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          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Body temperature increased                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (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  |                |                |                |
| Product administration error                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Humerus fracture                                |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood loss anaemia                              |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neutropenia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Abdominal pain                                  |                |                |                |



|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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          |
| Retroperitoneal haemorrhage                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastritis                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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          |
| Skin and subcutaneous tissue disorders          |               |                |                |
| Neutrophilic dermatosis                         |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |               |                |                |
| Cystitis noninfective                           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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 |               |                |                |
| Bone pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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          |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| Back pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Infections and infestations                     |               |                |                |
| Infection                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 1 / 1          | 1 / 1          |
| Epididymitis                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 23 (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          |
| COVID-19                                        |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumonia                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Part 1: Ruxolitinib + Siremadlin 30 mg | Part 1: Ruxolitinib + Rineterkib 200 mg | Part 1: Ruxolitinib + NIS793 |
|---------------------------------------------------------------------|----------------------------------------|-----------------------------------------|------------------------------|
| Total subjects affected by serious adverse events                   |                                        |                                         |                              |
| subjects affected / exposed                                         | 3 / 10 (30.00%)                        | 3 / 9 (33.33%)                          | 1 / 4 (25.00%)               |
| number of deaths (all causes)                                       | 0                                      | 1                                       | 0                            |
| number of deaths resulting from adverse events                      | 0                                      | 0                                       | 0                            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                        |                                         |                              |
| Prostate cancer                                                     |                                        |                                         |                              |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                         | 0 / 9 (0.00%)                           | 0 / 4 (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                                                  |                                        |                                         |                              |
| Aortic aneurysm rupture                                             |                                        |                                         |                              |

|                                                      |                |                |               |
|------------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed                          | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 1          | 0 / 0         |
| Haemorrhage                                          |                |                |               |
| subjects affected / exposed                          | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (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 |                |                |               |
| Multiple organ dysfunction syndrome                  |                |                |               |
| subjects affected / exposed                          | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (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 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (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         |
| Reproductive system and breast disorders             |                |                |               |
| Uterine prolapse                                     |                |                |               |
| subjects affected / exposed                          | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (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      |                |                |               |
| Acute respiratory failure                            |                |                |               |
| subjects affected / exposed                          | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (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         |
| Pulmonary embolism                                   |                |                |               |
| subjects affected / exposed                          | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (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                                       |                |                |               |
| Body temperature increased                           |                |                |               |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| 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  |                 |                |                |
| Product administration error                    |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (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          |
| Humerus fracture                                |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (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            |                 |                |                |
| Anaemia                                         |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (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 loss anaemia                              |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Neutropenia                                     |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                 |                |                |
| Abdominal pain                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (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          |
| Vomiting                                        |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (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          |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| Retroperitoneal haemorrhage                     |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (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          |
| Gastritis                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (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 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| 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          |                 |                |                |
| Neutrophilic dermatosis                         |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (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          |
| Renal and urinary disorders                     |                 |                |                |
| Cystitis noninfective                           |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (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          |
| Musculoskeletal and connective tissue disorders |                 |                |                |
| Bone pain                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (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          |
| Back pain                                       |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (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          |
| Infections and infestations                     |                 |                |                |
| Infection                                       |                 |                |                |

|                                                 |                |               |               |
|-------------------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%) | 0 / 4 (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         |
| Epididymitis                                    |                |               |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%) | 0 / 4 (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         |
| COVID-19                                        |                |               |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%) | 0 / 4 (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         |
| Pneumonia                                       |                |               |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%) | 0 / 4 (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>                                       | Part 1: Ruxolitinib + Crizanlizumab | Part 1: Ruxolitinib + Sabatolimab | Part 2: Ruxolitinib |
|---------------------------------------------------------------------|-------------------------------------|-----------------------------------|---------------------|
| Total subjects affected by serious adverse events                   |                                     |                                   |                     |
| subjects affected / exposed                                         | 1 / 6 (16.67%)                      | 1 / 2 (50.00%)                    | 0 / 1 (0.00%)       |
| number of deaths (all causes)                                       | 0                                   | 0                                 | 0                   |
| number of deaths resulting from adverse events                      | 0                                   | 0                                 | 0                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                                   |                     |
| Prostate cancer                                                     |                                     |                                   |                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                       | 0 / 2 (0.00%)                     | 0 / 1 (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                                                  |                                     |                                   |                     |
| Aortic aneurysm rupture                                             |                                     |                                   |                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                       | 0 / 2 (0.00%)                     | 0 / 1 (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               |
| Haemorrhage                                                         |                                     |                                   |                     |

|                                                      |               |               |               |
|------------------------------------------------------|---------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (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 |               |               |               |
| Multiple organ dysfunction syndrome                  |               |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (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 / 2 (0.00%) | 0 / 1 (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         |
| Reproductive system and breast disorders             |               |               |               |
| Uterine prolapse                                     |               |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (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      |               |               |               |
| Acute respiratory failure                            |               |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (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         |
| Pulmonary embolism                                   |               |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (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                                       |               |               |               |
| Body temperature increased                           |               |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (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       |               |               |               |
| Product administration error                         |               |               |               |

|                                                 |                |               |               |
|-------------------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (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         |
| Humerus fracture                                |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (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            |                |               |               |
| Anaemia                                         |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (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 loss anaemia                              |                |               |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (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         |
| Neutropenia                                     |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (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 / 2 (0.00%) | 0 / 1 (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 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (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         |
| Retroperitoneal haemorrhage                     |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (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         |
| Gastritis                                       |                |               |               |



|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 2 (50.00%) | 0 / 1 (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                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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         |
| Skin and subcutaneous tissue disorders          |               |                |               |
| Neutrophilic dermatosis                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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         |
| Renal and urinary disorders                     |               |                |               |
| Cystitis noninfective                           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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 |               |                |               |
| Bone pain                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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         |
| Back pain                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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                     |               |                |               |
| Infection                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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         |
| Epididymitis                                    |               |                |               |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 2 (50.00%) | 0 / 1 (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         |
| COVID-19                                        |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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         |
| Pneumonia                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 2 (0.00%)  | 0 / 1 (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>                                       | All Subjects     |  |  |
| Total subjects affected by serious adverse events                   |                  |  |  |
| subjects affected / exposed                                         | 15 / 45 (33.33%) |  |  |
| number of deaths (all causes)                                       | 4                |  |  |
| number of deaths resulting from adverse events                      | 1                |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Prostate cancer                                                     |                  |  |  |
| subjects affected / exposed                                         | 1 / 45 (2.22%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Vascular disorders                                                  |                  |  |  |
| Aortic aneurysm rupture                                             |                  |  |  |
| subjects affected / exposed                                         | 1 / 45 (2.22%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 1            |  |  |
| Haemorrhage                                                         |                  |  |  |
| subjects affected / exposed                                         | 1 / 45 (2.22%)   |  |  |
| occurrences causally related to treatment / all                     | 1 / 1            |  |  |
| deaths causally related to treatment / all                          | 1 / 1            |  |  |
| General disorders and administration site conditions                |                  |  |  |
| Multiple organ dysfunction syndrome                                 |                  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Pyrexia                                         |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Reproductive system and breast disorders        |                |  |  |
| Uterine prolapse                                |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Acute respiratory failure                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pulmonary embolism                              |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| Body temperature increased                      |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Product administration error                    |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Humerus fracture                                |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Blood and lymphatic system disorders</b>     |                |  |  |
| <b>Anaemia</b>                                  |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Blood loss anaemia</b>                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Neutropenia</b>                              |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Gastrointestinal disorders</b>               |                |  |  |
| <b>Abdominal pain</b>                           |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Vomiting</b>                                 |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Retroperitoneal haemorrhage</b>              |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Gastritis</b>                                |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Diarrhoea</b>                                |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Neutrophilic dermatosis                         |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Cystitis noninfective                           |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Bone pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Back pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Infection                                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |
| Epididymitis                                    |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| COVID-19                                        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumonia                                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                                   | Part 1: Ruxolitinib + Siremadlin 20 mg | Part 1: Ruxolitinib + Siremadlin 40 mg | Part 1: Ruxolitinib + Siremadlin |
|---------------------------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------|
| Total subjects affected by non-serious adverse events               |                                        |                                        |                                  |
| subjects affected / exposed                                         | 7 / 7 (100.00%)                        | 6 / 6 (100.00%)                        | 23 / 23 (100.00%)                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                        |                                        |                                  |
| Basal cell carcinoma                                                |                                        |                                        |                                  |
| subjects affected / exposed                                         | 0 / 7 (0.00%)                          | 1 / 6 (16.67%)                         | 1 / 23 (4.35%)                   |
| occurrences (all)                                                   | 0                                      | 2                                      | 2                                |
| Squamous cell carcinoma                                             |                                        |                                        |                                  |
| subjects affected / exposed                                         | 1 / 7 (14.29%)                         | 0 / 6 (0.00%)                          | 1 / 23 (4.35%)                   |
| occurrences (all)                                                   | 1                                      | 0                                      | 1                                |
| Squamous cell carcinoma of skin                                     |                                        |                                        |                                  |
| subjects affected / exposed                                         | 1 / 7 (14.29%)                         | 0 / 6 (0.00%)                          | 1 / 23 (4.35%)                   |
| occurrences (all)                                                   | 2                                      | 0                                      | 2                                |
| Vascular disorders                                                  |                                        |                                        |                                  |
| Capillary leak syndrome                                             |                                        |                                        |                                  |
| subjects affected / exposed                                         | 0 / 7 (0.00%)                          | 1 / 6 (16.67%)                         | 1 / 23 (4.35%)                   |
| occurrences (all)                                                   | 0                                      | 1                                      | 1                                |
| Angiopathy                                                          |                                        |                                        |                                  |
| subjects affected / exposed                                         | 0 / 7 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 23 (0.00%)                   |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                |
| Hypertension                                                        |                                        |                                        |                                  |
| subjects affected / exposed                                         | 4 / 7 (57.14%)                         | 0 / 6 (0.00%)                          | 4 / 23 (17.39%)                  |
| occurrences (all)                                                   | 4                                      | 0                                      | 4                                |
| Hypotension                                                         |                                        |                                        |                                  |

|                                                      |                |                |                 |
|------------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                                    | 1              | 0              | 1               |
| Venous thrombosis                                    |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)                                    | 0              | 1              | 1               |
| General disorders and administration site conditions |                |                |                 |
| Discomfort                                           |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)                                    | 0              | 1              | 1               |
| Chills                                               |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Chest pain                                           |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Asthenia                                             |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Chest discomfort                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Pyrexia                                              |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 2 / 6 (33.33%) | 5 / 23 (21.74%) |
| occurrences (all)                                    | 0              | 2              | 6               |
| Oedema peripheral                                    |                |                |                 |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 3 / 23 (13.04%) |
| occurrences (all)                                    | 1              | 1              | 3               |
| Mucosal inflammation                                 |                |                |                 |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                                    | 1              | 0              | 1               |
| Malaise                                              |                |                |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Fatigue                                              |                |                |                 |

|                                                                         |                      |                     |                       |
|-------------------------------------------------------------------------|----------------------|---------------------|-----------------------|
| subjects affected / exposed<br>occurrences (all)                        | 5 / 7 (71.43%)<br>10 | 2 / 6 (33.33%)<br>2 | 8 / 23 (34.78%)<br>15 |
| Respiratory, thoracic and mediastinal disorders                         |                      |                     |                       |
| Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  | 1 / 23 (4.35%)<br>2   |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)            | 1 / 7 (14.29%)<br>2  | 1 / 6 (16.67%)<br>1 | 2 / 23 (8.70%)<br>3   |
| Cough<br>subjects affected / exposed<br>occurrences (all)               | 2 / 7 (28.57%)<br>2  | 0 / 6 (0.00%)<br>0  | 2 / 23 (8.70%)<br>2   |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0   |
| Hypoxia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1 | 1 / 23 (4.35%)<br>1   |
| Nasal cavity mass<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0   |
| Psychiatric disorders                                                   |                      |                     |                       |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1 | 1 / 23 (4.35%)<br>1   |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1 | 1 / 23 (4.35%)<br>1   |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)      | 0 / 7 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1   |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0   | 2 / 6 (33.33%)<br>2 | 2 / 23 (8.70%)<br>2   |
| Investigations                                                          |                      |                     |                       |



|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| Alanine aminotransferase increased     |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 2 / 23 (8.70%) |
| occurrences (all)                      | 0              | 3              | 4              |
| Amylase increased                      |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 2 / 23 (8.70%) |
| occurrences (all)                      | 1              | 0              | 6              |
| Blood alkaline phosphatase increased   |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Blood creatine phosphokinase increased |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Blood creatinine increased             |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                      | 0              | 0              | 6              |
| Blood folate decreased                 |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Blood potassium increased              |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Neutrophil count decreased             |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                      | 2              | 0              | 2              |
| Lipase increased                       |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 2 / 23 (8.70%) |
| occurrences (all)                      | 1              | 0              | 7              |
| Heart sounds abnormal                  |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Heart rate decreased                   |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Cardiac murmur                         |                |                |                |

|                                                |                |                |                |
|------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 1              | 0              | 1              |
| White blood cell count decreased               |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)                              | 0              | 1              | 1              |
| Weight increased                               |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 2 / 23 (8.70%) |
| occurrences (all)                              | 0              | 1              | 2              |
| SARS-CoV-2 test positive                       |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Platelet count decreased                       |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 1              | 0              | 1              |
| Injury, poisoning and procedural complications |                |                |                |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Fall                                           |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Incorrect dose administered                    |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Ligament sprain                                |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 1              | 0              | 1              |
| Tendon rupture                                 |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 1              | 0              | 1              |
| Transfusion reaction                           |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                              | 0              | 0              | 2              |
| Skin abrasion                                  |                |                |                |

|                              |                |                |                |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| Skin wound                   |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)            | 0              | 0              | 1              |
| Cardiac disorders            |                |                |                |
| Atrial fibrillation          |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)            | 0              | 0              | 1              |
| Cardiac failure              |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| Palpitations                 |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| Pericardial effusion         |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| Sinus bradycardia            |                |                |                |
| subjects affected / exposed  | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)            | 1              | 0              | 1              |
| Supraventricular tachycardia |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)            | 0              | 0              | 0              |
| Nervous system disorders     |                |                |                |
| Dizziness                    |                |                |                |
| subjects affected / exposed  | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 2 / 23 (8.70%) |
| occurrences (all)            | 1              | 1              | 2              |
| Dysaesthesia                 |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)            | 0              | 1              | 1              |
| Dysgeusia                    |                |                |                |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 2 / 6 (33.33%) | 2 / 23 (8.70%) |
| occurrences (all)            | 0              | 4              | 4              |
| Headache                     |                |                |                |

|                                      |                |                 |                  |
|--------------------------------------|----------------|-----------------|------------------|
| subjects affected / exposed          | 3 / 7 (42.86%) | 0 / 6 (0.00%)   | 4 / 23 (17.39%)  |
| occurrences (all)                    | 3              | 0               | 4                |
| Migraine                             |                |                 |                  |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 6 (0.00%)   | 1 / 23 (4.35%)   |
| occurrences (all)                    | 1              | 0               | 1                |
| Sciatica                             |                |                 |                  |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 6 (0.00%)   | 1 / 23 (4.35%)   |
| occurrences (all)                    | 1              | 0               | 1                |
| Polyneuropathy                       |                |                 |                  |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)   | 0 / 23 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| Peripheral sensory neuropathy        |                |                 |                  |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)   | 1 / 23 (4.35%)   |
| occurrences (all)                    | 0              | 0               | 1                |
| Paraesthesia                         |                |                 |                  |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)   | 0 / 23 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| Blood and lymphatic system disorders |                |                 |                  |
| Anaemia                              |                |                 |                  |
| subjects affected / exposed          | 3 / 7 (42.86%) | 5 / 6 (83.33%)  | 15 / 23 (65.22%) |
| occurrences (all)                    | 3              | 19              | 31               |
| Lymphopenia                          |                |                 |                  |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 6 (0.00%)   | 2 / 23 (8.70%)   |
| occurrences (all)                    | 1              | 0               | 2                |
| Neutropenia                          |                |                 |                  |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 3 / 6 (50.00%)  | 11 / 23 (47.83%) |
| occurrences (all)                    | 0              | 4               | 18               |
| Splenomegaly                         |                |                 |                  |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)   | 0 / 23 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| Thrombocytopenia                     |                |                 |                  |
| subjects affected / exposed          | 1 / 7 (14.29%) | 6 / 6 (100.00%) | 14 / 23 (60.87%) |
| occurrences (all)                    | 1              | 16              | 29               |
| Eye disorders                        |                |                 |                  |
| Dry eye                              |                |                 |                  |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Erythema of eyelid          |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Eye pain                    |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Macular oedema              |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Photopsia                   |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal haemorrhage         |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 2              | 2              |
| Retinal detachment          |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Presbyopia                  |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)           | 1              | 0              | 1              |
| Visual impairment           |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 1              | 1              |
| Visual acuity reduced       |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Serous retinopathy          |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Retinopathy                 |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal disorders  |                |                |                |

|                             |                |                |                  |
|-----------------------------|----------------|----------------|------------------|
| Abdominal discomfort        |                |                |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)   |
| occurrences (all)           | 0              | 1              | 1                |
| Abdominal pain upper        |                |                |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 2 / 23 (8.70%)   |
| occurrences (all)           | 2              | 0              | 3                |
| Constipation                |                |                |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 4 / 23 (17.39%)  |
| occurrences (all)           | 3              | 3              | 8                |
| Diarrhoea                   |                |                |                  |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 6 (0.00%)  | 5 / 23 (21.74%)  |
| occurrences (all)           | 6              | 0              | 9                |
| Abdominal pain              |                |                |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 2 / 23 (8.70%)   |
| occurrences (all)           | 1              | 0              | 2                |
| Dry mouth                   |                |                |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| Abdominal distension        |                |                |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)   |
| occurrences (all)           | 0              | 0              | 1                |
| Flatulence                  |                |                |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)   |
| occurrences (all)           | 1              | 0              | 1                |
| Gingival bleeding           |                |                |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| Vomiting                    |                |                |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 3 / 23 (13.04%)  |
| occurrences (all)           | 1              | 0              | 3                |
| Oral dysaesthesia           |                |                |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)   |
| occurrences (all)           | 0              | 1              | 1                |
| Nausea                      |                |                |                  |
| subjects affected / exposed | 6 / 7 (85.71%) | 3 / 6 (50.00%) | 13 / 23 (56.52%) |
| occurrences (all)           | 16             | 11             | 34               |

|                                                                          |                     |                     |                     |
|--------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Mouth haemorrhage<br>subjects affected / exposed<br>occurrences (all)    | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders                                   |                     |                     |                     |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Blister<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)             | 1 / 7 (14.29%)<br>1 | 0 / 6 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1 |
| Actinic keratosis<br>subjects affected / exposed<br>occurrences (all)    | 1 / 7 (14.29%)<br>1 | 0 / 6 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1 |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)         | 1 / 7 (14.29%)<br>2 | 1 / 6 (16.67%)<br>3 | 2 / 23 (8.70%)<br>5 |
| Rash<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1 |
| Pain of skin<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0 |
| Skin discolouration                                                      |                     |                     |                     |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Skin disorder                                   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Skin lesion                                     |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Skin ulcer                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Trichodysplasia spinulosa                       |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Renal and urinary disorders                     |                |                |                |
| Renal failure                                   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Dysuria                                         |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Endocrine disorders                             |                |                |                |
| Hyperthyroidism                                 |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Gouty arthritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Bone pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                               | 2              | 0              | 2              |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Arthropathy                                     |                |                |                |



|                              |                |                |                 |
|------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed  | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)            | 1              | 0              | 1               |
| Arthralgia                   |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)            | 0              | 2              | 2               |
| Muscle spasms                |                |                |                 |
| subjects affected / exposed  | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)            | 1              | 0              | 1               |
| Muscle tightness             |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)            | 0              | 1              | 1               |
| Muscular weakness            |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)            | 0              | 0              | 0               |
| Pain in extremity            |                |                |                 |
| subjects affected / exposed  | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)            | 1              | 0              | 1               |
| Sacroiliac joint dysfunction |                |                |                 |
| subjects affected / exposed  | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)            | 1              | 0              | 1               |
| Infections and infestations  |                |                |                 |
| Bronchitis                   |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)            | 0              | 0              | 0               |
| Candida infection            |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)            | 0              | 0              | 0               |
| COVID-19                     |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 3 / 23 (13.04%) |
| occurrences (all)            | 0              | 1              | 3               |
| Erysipelas                   |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)            | 0              | 0              | 1               |
| Furuncle                     |                |                |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)            | 0              | 0              | 1               |

|                                    |                |                |                 |
|------------------------------------|----------------|----------------|-----------------|
| Eye infection                      |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0               |
| Upper respiratory tract infection  |                |                |                 |
| subjects affected / exposed        | 2 / 7 (28.57%) | 0 / 6 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)                  | 2              | 0              | 2               |
| Tooth infection                    |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0               |
| Oral herpes                        |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                  | 0              | 0              | 1               |
| Nasopharyngitis                    |                |                |                 |
| subjects affected / exposed        | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                  | 1              | 0              | 1               |
| Mucosal infection                  |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                  | 0              | 0              | 3               |
| Wound infection                    |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)                  | 0              | 1              | 1               |
| Urinary tract infection            |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                  | 0              | 0              | 1               |
| Metabolism and nutrition disorders |                |                |                 |
| Decreased appetite                 |                |                |                 |
| subjects affected / exposed        | 3 / 7 (42.86%) | 0 / 6 (0.00%)  | 3 / 23 (13.04%) |
| occurrences (all)                  | 5              | 0              | 5               |
| Dehydration                        |                |                |                 |
| subjects affected / exposed        | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                  | 1              | 0              | 1               |
| Gout                               |                |                |                 |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0               |
| Hyperkalaemia                      |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 1              | 0              | 2               |
| Hyperuricaemia              |                |                |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 4 / 23 (17.39%) |
| occurrences (all)           | 1              | 1              | 4               |
| Hypokalaemia                |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 1              | 1               |
| Hyponatraemia               |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Iron overload               |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 1              | 1               |

| <b>Non-serious adverse events</b>                                   | Part 1: Ruxolitinib + Siremadlin 30 mg | Part 1: Ruxolitinib + Rineterkib 200 mg | Part 1: Ruxolitinib + NIS793 |
|---------------------------------------------------------------------|----------------------------------------|-----------------------------------------|------------------------------|
| Total subjects affected by non-serious adverse events               |                                        |                                         |                              |
| subjects affected / exposed                                         | 10 / 10 (100.00%)                      | 9 / 9 (100.00%)                         | 3 / 4 (75.00%)               |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                        |                                         |                              |
| Basal cell carcinoma                                                |                                        |                                         |                              |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                         | 0 / 9 (0.00%)                           | 1 / 4 (25.00%)               |
| occurrences (all)                                                   | 0                                      | 0                                       | 2                            |
| Squamous cell carcinoma                                             |                                        |                                         |                              |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                         | 0 / 9 (0.00%)                           | 0 / 4 (0.00%)                |
| occurrences (all)                                                   | 0                                      | 0                                       | 0                            |
| Squamous cell carcinoma of skin                                     |                                        |                                         |                              |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                         | 0 / 9 (0.00%)                           | 0 / 4 (0.00%)                |
| occurrences (all)                                                   | 0                                      | 0                                       | 0                            |
| Vascular disorders                                                  |                                        |                                         |                              |
| Capillary leak syndrome                                             |                                        |                                         |                              |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                         | 0 / 9 (0.00%)                           | 0 / 4 (0.00%)                |
| occurrences (all)                                                   | 0                                      | 0                                       | 0                            |
| Angiopathy                                                          |                                        |                                         |                              |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                         | 0 / 9 (0.00%)                           | 0 / 4 (0.00%)                |
| occurrences (all)                                                   | 0                                      | 0                                       | 0                            |
| Hypertension                                                        |                                        |                                         |                              |

|                                                      |                 |                |                |
|------------------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Hypotension                                          |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Venous thrombosis                                    |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| General disorders and administration site conditions |                 |                |                |
| Discomfort                                           |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Chills                                               |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 1 / 4 (25.00%) |
| occurrences (all)                                    | 0               | 1              | 1              |
| Chest pain                                           |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Asthenia                                             |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 3 / 9 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 3              | 0              |
| Chest discomfort                                     |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Pyrexia                                              |                 |                |                |
| subjects affected / exposed                          | 3 / 10 (30.00%) | 1 / 9 (11.11%) | 1 / 4 (25.00%) |
| occurrences (all)                                    | 4               | 2              | 1              |
| Oedema peripheral                                    |                 |                |                |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Mucosal inflammation                                 |                 |                |                |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Malaise                                              |                 |                |                |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0              |
| Fatigue                                         |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 3               | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                 |                |                |
| Dyspnoea exertional                             |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 2               | 0              | 0              |
| Dyspnoea                                        |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Cough                                           |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0              |
| Epistaxis                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 2 / 4 (50.00%) |
| occurrences (all)                               | 0               | 1              | 4              |
| Hypoxia                                         |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Nasal cavity mass                               |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                               | 0               | 0              | 1              |
| Psychiatric disorders                           |                 |                |                |
| Anxiety                                         |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Confusional state                               |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Sleep disorder                                  |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0              |
| Insomnia                                        |                 |                |                |

|                                                                                            |                      |                     |                     |
|--------------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                           | 0 / 10 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 1 / 4 (25.00%)<br>1 |
| Investigations                                                                             |                      |                     |                     |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)     | 1 / 10 (10.00%)<br>1 | 1 / 9 (11.11%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 10 (10.00%)<br>5 | 0 / 9 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 2 / 9 (22.22%)<br>2 | 0 / 4 (0.00%)<br>0  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 10 (10.00%)<br>6 | 1 / 9 (11.11%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Blood folate decreased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 10 (10.00%)<br>1 | 1 / 9 (11.11%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Blood potassium increased<br>subjects affected / exposed<br>occurrences (all)              | 0 / 10 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 10 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 10 (10.00%)<br>6 | 0 / 9 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Heart sounds abnormal<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 10 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Heart rate decreased                                                                       |                      |                     |                     |

|                                                |                 |                |                |
|------------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Cardiac murmur                                 |                 |                |                |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| White blood cell count decreased               |                 |                |                |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Weight increased                               |                 |                |                |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 1               | 0              | 0              |
| SARS-CoV-2 test positive                       |                 |                |                |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 1               | 0              | 0              |
| Platelet count decreased                       |                 |                |                |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Injury, poisoning and procedural complications |                 |                |                |
| Contusion                                      |                 |                |                |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                              | 1               | 0              | 2              |
| Fall                                           |                 |                |                |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 1              | 0              |
| Incorrect dose administered                    |                 |                |                |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 1               | 0              | 0              |
| Ligament sprain                                |                 |                |                |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Tendon rupture                                 |                 |                |                |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Transfusion reaction                           |                 |                |                |

|                              |                 |                |                |
|------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 2               | 0              | 0              |
| Skin abrasion                |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 1              | 0              |
| Skin wound                   |                 |                |                |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |
| Cardiac disorders            |                 |                |                |
| Atrial fibrillation          |                 |                |                |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |
| Cardiac failure              |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 1              | 0              |
| Palpitations                 |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)            | 0               | 0              | 1              |
| Pericardial effusion         |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Sinus bradycardia            |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Supraventricular tachycardia |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Nervous system disorders     |                 |                |                |
| Dizziness                    |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Dysaesthesia                 |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Dysgeusia                    |                 |                |                |



|                                      |                 |                |                |
|--------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 1 / 4 (25.00%) |
| occurrences (all)                    | 0               | 1              | 1              |
| Headache                             |                 |                |                |
| subjects affected / exposed          | 1 / 10 (10.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 1               | 1              | 0              |
| Migraine                             |                 |                |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Sciatica                             |                 |                |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Polyneuropathy                       |                 |                |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Peripheral sensory neuropathy        |                 |                |                |
| subjects affected / exposed          | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 1               | 0              | 0              |
| Paraesthesia                         |                 |                |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Blood and lymphatic system disorders |                 |                |                |
| Anaemia                              |                 |                |                |
| subjects affected / exposed          | 7 / 10 (70.00%) | 1 / 9 (11.11%) | 2 / 4 (50.00%) |
| occurrences (all)                    | 9               | 1              | 2              |
| Lymphopenia                          |                 |                |                |
| subjects affected / exposed          | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 1               | 0              | 0              |
| Neutropenia                          |                 |                |                |
| subjects affected / exposed          | 8 / 10 (80.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 14              | 0              | 0              |
| Splenomegaly                         |                 |                |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Thrombocytopenia                     |                 |                |                |
| subjects affected / exposed          | 7 / 10 (70.00%) | 2 / 9 (22.22%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 12              | 3              | 0              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Eye disorders               |                |                |                |
| Dry eye                     |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Erythema of eyelid          |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Eye pain                    |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Macular oedema              |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Photopsia                   |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal haemorrhage         |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal detachment          |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Presbyopia                  |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Visual impairment           |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Visual acuity reduced       |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Serous retinopathy          |                |                |                |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Retinopathy                 |                |                |                |

|                                                  |                     |                     |                    |
|--------------------------------------------------|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | 2 / 9 (22.22%)<br>2 | 0 / 4 (0.00%)<br>0 |
| Gastrointestinal disorders                       |                     |                     |                    |
| Abdominal discomfort                             |                     |                     |                    |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 1 / 9 (11.11%)      | 0 / 4 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Abdominal pain upper                             |                     |                     |                    |
| subjects affected / exposed                      | 1 / 10 (10.00%)     | 0 / 9 (0.00%)       | 0 / 4 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                  |
| Constipation                                     |                     |                     |                    |
| subjects affected / exposed                      | 2 / 10 (20.00%)     | 1 / 9 (11.11%)      | 0 / 4 (0.00%)      |
| occurrences (all)                                | 2                   | 1                   | 0                  |
| Diarrhoea                                        |                     |                     |                    |
| subjects affected / exposed                      | 2 / 10 (20.00%)     | 6 / 9 (66.67%)      | 0 / 4 (0.00%)      |
| occurrences (all)                                | 3                   | 6                   | 0                  |
| Abdominal pain                                   |                     |                     |                    |
| subjects affected / exposed                      | 1 / 10 (10.00%)     | 0 / 9 (0.00%)       | 0 / 4 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                  |
| Dry mouth                                        |                     |                     |                    |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 1 / 9 (11.11%)      | 1 / 4 (25.00%)     |
| occurrences (all)                                | 0                   | 1                   | 1                  |
| Abdominal distension                             |                     |                     |                    |
| subjects affected / exposed                      | 1 / 10 (10.00%)     | 0 / 9 (0.00%)       | 0 / 4 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                  |
| Flatulence                                       |                     |                     |                    |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 9 (0.00%)       | 0 / 4 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Gingival bleeding                                |                     |                     |                    |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 1 / 9 (11.11%)      | 0 / 4 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Vomiting                                         |                     |                     |                    |
| subjects affected / exposed                      | 2 / 10 (20.00%)     | 1 / 9 (11.11%)      | 0 / 4 (0.00%)      |
| occurrences (all)                                | 2                   | 4                   | 0                  |
| Oral dysaesthesia                                |                     |                     |                    |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 9 (0.00%)       | 0 / 4 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |

|                                        |                 |                |                |
|----------------------------------------|-----------------|----------------|----------------|
| Nausea                                 |                 |                |                |
| subjects affected / exposed            | 4 / 10 (40.00%) | 3 / 9 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 7               | 3              | 0              |
| Mouth haemorrhage                      |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                      | 0               | 0              | 1              |
| Skin and subcutaneous tissue disorders |                 |                |                |
| Dry skin                               |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Dermatitis acneiform                   |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 1              | 0              |
| Blister                                |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Alopecia                               |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Actinic keratosis                      |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Night sweats                           |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                      | 0               | 0              | 1              |
| Rash                                   |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 2 / 9 (22.22%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 2              | 0              |
| Pruritus                               |                 |                |                |
| subjects affected / exposed            | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                      | 1               | 0              | 1              |
| Pain of skin                           |                 |                |                |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0               | 1              | 0              |
| Rash maculo-papular                    |                 |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Skin discolouration                             |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Skin disorder                                   |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Skin lesion                                     |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Skin ulcer                                      |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Trichodysplasia spinulosa                       |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Renal and urinary disorders                     |                |                |                |
| Renal failure                                   |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Dysuria                                         |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Endocrine disorders                             |                |                |                |
| Hyperthyroidism                                 |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Gouty arthritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Bone pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 2 / 9 (22.22%) | 1 / 4 (25.00%) |
| occurrences (all)                               | 0              | 2              | 1              |
| Back pain                                       |                |                |                |

|                              |                 |                |                |
|------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Arthropathy                  |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Arthralgia                   |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 2 / 9 (22.22%) | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 3              | 0              |
| Muscle spasms                |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 1 / 4 (25.00%) |
| occurrences (all)            | 0               | 1              | 2              |
| Muscle tightness             |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Muscular weakness            |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 1              | 0              |
| Pain in extremity            |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Sacroiliac joint dysfunction |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Infections and infestations  |                 |                |                |
| Bronchitis                   |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)            | 0               | 1              | 0              |
| Candida infection            |                 |                |                |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)            | 0               | 0              | 1              |
| COVID-19                     |                 |                |                |
| subjects affected / exposed  | 2 / 10 (20.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 2               | 0              | 0              |
| Erysipelas                   |                 |                |                |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| Furuncle                           |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0              |
| Eye infection                      |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Upper respiratory tract infection  |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Tooth infection                    |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Oral herpes                        |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0              |
| Nasopharyngitis                    |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0               | 1              | 0              |
| Mucosal infection                  |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 3               | 0              | 0              |
| Wound infection                    |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Urinary tract infection            |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                  | 1               | 1              | 0              |
| Metabolism and nutrition disorders |                 |                |                |
| Decreased appetite                 |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 9 (11.11%) | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0               | 1              | 0              |
| Dehydration                        |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Gout                               |                 |                |                |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Hyperkalaemia               |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Hyperuricaemia              |                 |                |               |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 9 (11.11%) | 0 / 4 (0.00%) |
| occurrences (all)           | 2               | 1              | 0             |
| Hypokalaemia                |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Hyponatraemia               |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 9 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Iron overload               |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 9 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |

| <b>Non-serious adverse events</b>                                   | Part 1: Ruxolitinib + Crizanlizumab | Part 1: Ruxolitinib + Sabatolimab | Part 2: Ruxolitinib |
|---------------------------------------------------------------------|-------------------------------------|-----------------------------------|---------------------|
| Total subjects affected by non-serious adverse events               |                                     |                                   |                     |
| subjects affected / exposed                                         | 6 / 6 (100.00%)                     | 2 / 2 (100.00%)                   | 0 / 1 (0.00%)       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                                   |                     |
| Basal cell carcinoma                                                |                                     |                                   |                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                       | 0 / 2 (0.00%)                     | 0 / 1 (0.00%)       |
| occurrences (all)                                                   | 0                                   | 0                                 | 0                   |
| Squamous cell carcinoma                                             |                                     |                                   |                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                       | 0 / 2 (0.00%)                     | 0 / 1 (0.00%)       |
| occurrences (all)                                                   | 0                                   | 0                                 | 0                   |
| Squamous cell carcinoma of skin                                     |                                     |                                   |                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                       | 0 / 2 (0.00%)                     | 0 / 1 (0.00%)       |
| occurrences (all)                                                   | 0                                   | 0                                 | 0                   |
| Vascular disorders                                                  |                                     |                                   |                     |
| Capillary leak syndrome                                             |                                     |                                   |                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                       | 0 / 2 (0.00%)                     | 0 / 1 (0.00%)       |
| occurrences (all)                                                   | 0                                   | 0                                 | 0                   |
| Angiopathy                                                          |                                     |                                   |                     |



|                                                      |                |               |               |
|------------------------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 1              | 0             | 0             |
| Hypertension                                         |                |               |               |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 1              | 0             | 0             |
| Hypotension                                          |                |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 0              | 0             | 0             |
| Venous thrombosis                                    |                |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 0              | 0             | 0             |
| General disorders and administration site conditions |                |               |               |
| Discomfort                                           |                |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 0              | 0             | 0             |
| Chills                                               |                |               |               |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 0              | 0             | 0             |
| Chest pain                                           |                |               |               |
| subjects affected / exposed                          | 2 / 6 (33.33%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 2              | 0             | 0             |
| Asthenia                                             |                |               |               |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 2              | 0             | 0             |
| Chest discomfort                                     |                |               |               |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 1              | 0             | 0             |
| Pyrexia                                              |                |               |               |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 1              | 0             | 0             |
| Oedema peripheral                                    |                |               |               |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                                    | 2              | 0             | 0             |
| Mucosal inflammation                                 |                |               |               |

|                                                                                                                            |                     |                    |                    |
|----------------------------------------------------------------------------------------------------------------------------|---------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)                                                                           | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Malaise<br>subjects affected / exposed<br>occurrences (all)                                                                | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                                | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                               | 2 / 6 (33.33%)<br>2 | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                                                              | 1 / 6 (16.67%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Hypoxia<br>subjects affected / exposed<br>occurrences (all)                                                                | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Nasal cavity mass<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Sleep disorder                                                                                                             |                     |                    |                    |

|                                        |                |               |               |
|----------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Insomnia                               |                |               |               |
| subjects affected / exposed            | 2 / 6 (33.33%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 2              | 0             | 0             |
| Investigations                         |                |               |               |
| Alanine aminotransferase increased     |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Amylase increased                      |                |               |               |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Blood alkaline phosphatase increased   |                |               |               |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Blood creatine phosphokinase increased |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Blood creatinine increased             |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Blood folate decreased                 |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Blood potassium increased              |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Neutrophil count decreased             |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Lipase increased                       |                |               |               |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Heart sounds abnormal                  |                |               |               |

|                                                |                |               |               |
|------------------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 0             | 0             |
| Heart rate decreased                           |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Cardiac murmur                                 |                |               |               |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 2              | 0             | 0             |
| White blood cell count decreased               |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Weight increased                               |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| SARS-CoV-2 test positive                       |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Platelet count decreased                       |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Injury, poisoning and procedural complications |                |               |               |
| Contusion                                      |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Fall                                           |                |               |               |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 0             | 0             |
| Incorrect dose administered                    |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Ligament sprain                                |                |               |               |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Tendon rupture                                 |                |               |               |

|                              |                |               |               |
|------------------------------|----------------|---------------|---------------|
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Transfusion reaction         |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Skin abrasion                |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Skin wound                   |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Cardiac disorders            |                |               |               |
| Atrial fibrillation          |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Cardiac failure              |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Palpitations                 |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Pericardial effusion         |                |               |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Sinus bradycardia            |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Supraventricular tachycardia |                |               |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Nervous system disorders     |                |               |               |
| Dizziness                    |                |               |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 2              | 0             | 0             |
| Dysaesthesia                 |                |               |               |

|                                      |                |               |               |
|--------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Dysgeusia                            |                |               |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Headache                             |                |               |               |
| subjects affected / exposed          | 2 / 6 (33.33%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 3              | 0             | 0             |
| Migraine                             |                |               |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Sciatica                             |                |               |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Polyneuropathy                       |                |               |               |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Peripheral sensory neuropathy        |                |               |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Paraesthesia                         |                |               |               |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Blood and lymphatic system disorders |                |               |               |
| Anaemia                              |                |               |               |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Lymphopenia                          |                |               |               |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Neutropenia                          |                |               |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Splenomegaly                         |                |               |               |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |

|                                                                           |                     |                      |                    |
|---------------------------------------------------------------------------|---------------------|----------------------|--------------------|
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)      | 1 / 6 (16.67%)<br>2 | 2 / 2 (100.00%)<br>2 | 0 / 1 (0.00%)<br>0 |
| Eye disorders                                                             |                     |                      |                    |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Erythema of eyelid<br>subjects affected / exposed<br>occurrences (all)    | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Eye pain<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Macular oedema<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Photopsia<br>subjects affected / exposed<br>occurrences (all)             | 1 / 6 (16.67%)<br>2 | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Retinal haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Retinal detachment<br>subjects affected / exposed<br>occurrences (all)    | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Presbyopia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Visual impairment<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Visual acuity reduced<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0 |
| Serous retinopathy                                                        |                     |                      |                    |

|                             |                |               |               |
|-----------------------------|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Retinopathy                 |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Gastrointestinal disorders  |                |               |               |
| Abdominal discomfort        |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Abdominal pain upper        |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Constipation                |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Diarrhoea                   |                |               |               |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 5              | 0             | 0             |
| Abdominal pain              |                |               |               |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Dry mouth                   |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Abdominal distension        |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Flatulence                  |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Gingival bleeding           |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Vomiting                    |                |               |               |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 0             | 0             |



|                                        |                |               |               |
|----------------------------------------|----------------|---------------|---------------|
| Oral dysaesthesia                      |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Nausea                                 |                |               |               |
| subjects affected / exposed            | 2 / 6 (33.33%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 2              | 0             | 0             |
| Mouth haemorrhage                      |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Skin and subcutaneous tissue disorders |                |               |               |
| Dry skin                               |                |               |               |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Dermatitis acneiform                   |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Blister                                |                |               |               |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Alopecia                               |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Actinic keratosis                      |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Night sweats                           |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Rash                                   |                |               |               |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Pruritus                               |                |               |               |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Pain of skin                           |                |               |               |

|                                                 |                |               |               |
|-------------------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Rash maculo-papular                             |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Skin discolouration                             |                |               |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 0             | 0             |
| Skin disorder                                   |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Skin lesion                                     |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Skin ulcer                                      |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Trichodysplasia spinulosa                       |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Renal and urinary disorders                     |                |               |               |
| Renal failure                                   |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Dysuria                                         |                |               |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| Endocrine disorders                             |                |               |               |
| Hyperthyroidism                                 |                |               |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 0             | 0             |
| Musculoskeletal and connective tissue disorders |                |               |               |
| Gouty arthritis                                 |                |               |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 2              | 0             | 0             |
| Bone pain                                       |                |               |               |

|                              |                |               |               |
|------------------------------|----------------|---------------|---------------|
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Back pain                    |                |               |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Arthropathy                  |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Arthralgia                   |                |               |               |
| subjects affected / exposed  | 2 / 6 (33.33%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 3              | 0             | 0             |
| Muscle spasms                |                |               |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Muscle tightness             |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Muscular weakness            |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Pain in extremity            |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Sacroiliac joint dysfunction |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Infections and infestations  |                |               |               |
| Bronchitis                   |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Candida infection            |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| COVID-19                     |                |               |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |

|                                    |               |               |               |
|------------------------------------|---------------|---------------|---------------|
| Erysipelas                         |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Furuncle                           |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Eye infection                      |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Upper respiratory tract infection  |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Tooth infection                    |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Oral herpes                        |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Nasopharyngitis                    |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Mucosal infection                  |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Wound infection                    |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Urinary tract infection            |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Metabolism and nutrition disorders |               |               |               |
| Decreased appetite                 |               |               |               |
| subjects affected / exposed        | 0 / 6 (0.00%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0             | 0             | 0             |
| Dehydration                        |               |               |               |

|                             |                |               |               |
|-----------------------------|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Gout                        |                |               |               |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Hyperkalaemia               |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Hyperuricaemia              |                |               |               |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Hypokalaemia                |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Hyponatraemia               |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Iron overload               |                |               |               |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 2 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | All Subjects     |  |  |
|---------------------------------------------------------------------|------------------|--|--|
| Total subjects affected by non-serious adverse events               |                  |  |  |
| subjects affected / exposed                                         | 43 / 45 (95.56%) |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Basal cell carcinoma                                                |                  |  |  |
| subjects affected / exposed                                         | 2 / 45 (4.44%)   |  |  |
| occurrences (all)                                                   | 4                |  |  |
| Squamous cell carcinoma                                             |                  |  |  |
| subjects affected / exposed                                         | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                                                   | 1                |  |  |
| Squamous cell carcinoma of skin                                     |                  |  |  |
| subjects affected / exposed                                         | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                                                   | 2                |  |  |
| Vascular disorders                                                  |                  |  |  |

|                                                                             |                       |  |  |
|-----------------------------------------------------------------------------|-----------------------|--|--|
| Capillary leak syndrome<br>subjects affected / exposed<br>occurrences (all) | 1 / 45 (2.22%)<br>1   |  |  |
| Angiopathy<br>subjects affected / exposed<br>occurrences (all)              | 1 / 45 (2.22%)<br>1   |  |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)            | 5 / 45 (11.11%)<br>5  |  |  |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)             | 1 / 45 (2.22%)<br>1   |  |  |
| Venous thrombosis<br>subjects affected / exposed<br>occurrences (all)       | 1 / 45 (2.22%)<br>1   |  |  |
| General disorders and administration<br>site conditions                     |                       |  |  |
| Discomfort<br>subjects affected / exposed<br>occurrences (all)              | 1 / 45 (2.22%)<br>1   |  |  |
| Chills<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 45 (4.44%)<br>2   |  |  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)              | 2 / 45 (4.44%)<br>2   |  |  |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                | 4 / 45 (8.89%)<br>5   |  |  |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)        | 1 / 45 (2.22%)<br>1   |  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                 | 8 / 45 (17.78%)<br>10 |  |  |
| Oedema peripheral                                                           |                       |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                           |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mucosal inflammation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Malaise</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                       | <p>4 / 45 (8.89%)</p> <p>5</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>8 / 45 (17.78%)</p> <p>15</p>                                                             |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Dyspnoea exertional</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypoxia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal cavity mass</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 45 (4.44%)</p> <p>3</p> <p>4 / 45 (8.89%)</p> <p>5</p> <p>3 / 45 (6.67%)</p> <p>3</p> <p>4 / 45 (8.89%)</p> <p>6</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>1 / 45 (2.22%)</p> <p>1</p> |  |  |
| <p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Confusional state</p>                                                                                                                                                                                                                                                                                                                                                                                                                | <p>1 / 45 (2.22%)</p> <p>1</p>                                                                                                                                                            |  |  |

|                                        |                 |  |  |
|----------------------------------------|-----------------|--|--|
| subjects affected / exposed            | 1 / 45 (2.22%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Sleep disorder                         |                 |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Insomnia                               |                 |  |  |
| subjects affected / exposed            | 6 / 45 (13.33%) |  |  |
| occurrences (all)                      | 6               |  |  |
| Investigations                         |                 |  |  |
| Alanine aminotransferase increased     |                 |  |  |
| subjects affected / exposed            | 3 / 45 (6.67%)  |  |  |
| occurrences (all)                      | 5               |  |  |
| Amylase increased                      |                 |  |  |
| subjects affected / exposed            | 3 / 45 (6.67%)  |  |  |
| occurrences (all)                      | 7               |  |  |
| Blood alkaline phosphatase increased   |                 |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Blood creatine phosphokinase increased |                 |  |  |
| subjects affected / exposed            | 3 / 45 (6.67%)  |  |  |
| occurrences (all)                      | 3               |  |  |
| Blood creatinine increased             |                 |  |  |
| subjects affected / exposed            | 2 / 45 (4.44%)  |  |  |
| occurrences (all)                      | 7               |  |  |
| Blood folate decreased                 |                 |  |  |
| subjects affected / exposed            | 2 / 45 (4.44%)  |  |  |
| occurrences (all)                      | 2               |  |  |
| Blood potassium increased              |                 |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Neutrophil count decreased             |                 |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)  |  |  |
| occurrences (all)                      | 2               |  |  |
| Lipase increased                       |                 |  |  |



|                                                |                |  |  |
|------------------------------------------------|----------------|--|--|
| subjects affected / exposed                    | 3 / 45 (6.67%) |  |  |
| occurrences (all)                              | 8              |  |  |
| Heart sounds abnormal                          |                |  |  |
| subjects affected / exposed                    | 1 / 45 (2.22%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Heart rate decreased                           |                |  |  |
| subjects affected / exposed                    | 1 / 45 (2.22%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Cardiac murmur                                 |                |  |  |
| subjects affected / exposed                    | 2 / 45 (4.44%) |  |  |
| occurrences (all)                              | 3              |  |  |
| White blood cell count decreased               |                |  |  |
| subjects affected / exposed                    | 1 / 45 (2.22%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Weight increased                               |                |  |  |
| subjects affected / exposed                    | 2 / 45 (4.44%) |  |  |
| occurrences (all)                              | 2              |  |  |
| SARS-CoV-2 test positive                       |                |  |  |
| subjects affected / exposed                    | 1 / 45 (2.22%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Platelet count decreased                       |                |  |  |
| subjects affected / exposed                    | 1 / 45 (2.22%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Injury, poisoning and procedural complications |                |  |  |
| Contusion                                      |                |  |  |
| subjects affected / exposed                    | 2 / 45 (4.44%) |  |  |
| occurrences (all)                              | 3              |  |  |
| Fall                                           |                |  |  |
| subjects affected / exposed                    | 2 / 45 (4.44%) |  |  |
| occurrences (all)                              | 2              |  |  |
| Incorrect dose administered                    |                |  |  |
| subjects affected / exposed                    | 1 / 45 (2.22%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Ligament sprain                                |                |  |  |

|                              |                |  |  |
|------------------------------|----------------|--|--|
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Tendon rupture               |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Transfusion reaction         |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 2              |  |  |
| Skin abrasion                |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Skin wound                   |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Cardiac disorders            |                |  |  |
| Atrial fibrillation          |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Cardiac failure              |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Palpitations                 |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Pericardial effusion         |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Sinus bradycardia            |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Supraventricular tachycardia |                |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%) |  |  |
| occurrences (all)            | 1              |  |  |
| Nervous system disorders     |                |  |  |
| Dizziness                    |                |  |  |

|                                      |                  |  |  |
|--------------------------------------|------------------|--|--|
| subjects affected / exposed          | 3 / 45 (6.67%)   |  |  |
| occurrences (all)                    | 4                |  |  |
| Dysaesthesia                         |                  |  |  |
| subjects affected / exposed          | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Dysgeusia                            |                  |  |  |
| subjects affected / exposed          | 4 / 45 (8.89%)   |  |  |
| occurrences (all)                    | 6                |  |  |
| Headache                             |                  |  |  |
| subjects affected / exposed          | 7 / 45 (15.56%)  |  |  |
| occurrences (all)                    | 8                |  |  |
| Migraine                             |                  |  |  |
| subjects affected / exposed          | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Sciatica                             |                  |  |  |
| subjects affected / exposed          | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Polyneuropathy                       |                  |  |  |
| subjects affected / exposed          | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Peripheral sensory neuropathy        |                  |  |  |
| subjects affected / exposed          | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Paraesthesia                         |                  |  |  |
| subjects affected / exposed          | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Blood and lymphatic system disorders |                  |  |  |
| Anaemia                              |                  |  |  |
| subjects affected / exposed          | 19 / 45 (42.22%) |  |  |
| occurrences (all)                    | 35               |  |  |
| Lymphopenia                          |                  |  |  |
| subjects affected / exposed          | 3 / 45 (6.67%)   |  |  |
| occurrences (all)                    | 3                |  |  |
| Neutropenia                          |                  |  |  |
| subjects affected / exposed          | 11 / 45 (24.44%) |  |  |
| occurrences (all)                    | 18               |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| Splenomegaly                |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Thrombocytopenia            |                  |  |  |
| subjects affected / exposed | 19 / 45 (42.22%) |  |  |
| occurrences (all)           | 36               |  |  |
| Eye disorders               |                  |  |  |
| Dry eye                     |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Erythema of eyelid          |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Eye pain                    |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Macular oedema              |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Photopsia                   |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Retinal haemorrhage         |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Retinal detachment          |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Presbyopia                  |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Visual impairment           |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Visual acuity reduced       |                  |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Serous retinopathy          |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Retinopathy                 |                  |  |  |
| subjects affected / exposed | 2 / 45 (4.44%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Gastrointestinal disorders  |                  |  |  |
| Abdominal discomfort        |                  |  |  |
| subjects affected / exposed | 2 / 45 (4.44%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Abdominal pain upper        |                  |  |  |
| subjects affected / exposed | 2 / 45 (4.44%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Constipation                |                  |  |  |
| subjects affected / exposed | 5 / 45 (11.11%)  |  |  |
| occurrences (all)           | 9                |  |  |
| Diarrhoea                   |                  |  |  |
| subjects affected / exposed | 13 / 45 (28.89%) |  |  |
| occurrences (all)           | 20               |  |  |
| Abdominal pain              |                  |  |  |
| subjects affected / exposed | 3 / 45 (6.67%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Dry mouth                   |                  |  |  |
| subjects affected / exposed | 2 / 45 (4.44%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Abdominal distension        |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Flatulence                  |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Gingival bleeding           |                  |  |  |
| subjects affected / exposed | 1 / 45 (2.22%)   |  |  |
| occurrences (all)           | 1                |  |  |

|                                        |                  |  |  |
|----------------------------------------|------------------|--|--|
| Vomiting                               |                  |  |  |
| subjects affected / exposed            | 5 / 45 (11.11%)  |  |  |
| occurrences (all)                      | 9                |  |  |
| Oral dysaesthesia                      |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Nausea                                 |                  |  |  |
| subjects affected / exposed            | 18 / 45 (40.00%) |  |  |
| occurrences (all)                      | 39               |  |  |
| Mouth haemorrhage                      |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Skin and subcutaneous tissue disorders |                  |  |  |
| Dry skin                               |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Dermatitis acneiform                   |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Blister                                |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Alopecia                               |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Actinic keratosis                      |                  |  |  |
| subjects affected / exposed            | 1 / 45 (2.22%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Night sweats                           |                  |  |  |
| subjects affected / exposed            | 3 / 45 (6.67%)   |  |  |
| occurrences (all)                      | 6                |  |  |
| Rash                                   |                  |  |  |
| subjects affected / exposed            | 2 / 45 (4.44%)   |  |  |
| occurrences (all)                      | 2                |  |  |
| Pruritus                               |                  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 3 / 45 (6.67%) |  |  |
| occurrences (all)                               | 3              |  |  |
| Pain of skin                                    |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Rash maculo-papular                             |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Skin discolouration                             |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Skin disorder                                   |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Skin lesion                                     |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Skin ulcer                                      |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Trichodysplasia spinulosa                       |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Renal and urinary disorders                     |                |  |  |
| Renal failure                                   |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Dysuria                                         |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Endocrine disorders                             |                |  |  |
| Hyperthyroidism                                 |                |  |  |
| subjects affected / exposed                     | 1 / 45 (2.22%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |

|                              |                 |  |  |
|------------------------------|-----------------|--|--|
| Gouty arthritis              |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 2               |  |  |
| Bone pain                    |                 |  |  |
| subjects affected / exposed  | 5 / 45 (11.11%) |  |  |
| occurrences (all)            | 6               |  |  |
| Back pain                    |                 |  |  |
| subjects affected / exposed  | 2 / 45 (4.44%)  |  |  |
| occurrences (all)            | 2               |  |  |
| Arthropathy                  |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Arthralgia                   |                 |  |  |
| subjects affected / exposed  | 5 / 45 (11.11%) |  |  |
| occurrences (all)            | 8               |  |  |
| Muscle spasms                |                 |  |  |
| subjects affected / exposed  | 4 / 45 (8.89%)  |  |  |
| occurrences (all)            | 5               |  |  |
| Muscle tightness             |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Muscular weakness            |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Pain in extremity            |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Sacroiliac joint dysfunction |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Infections and infestations  |                 |  |  |
| Bronchitis                   |                 |  |  |
| subjects affected / exposed  | 1 / 45 (2.22%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Candida infection            |                 |  |  |



|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| COVID-19                           |                |  |  |
| subjects affected / exposed        | 3 / 45 (6.67%) |  |  |
| occurrences (all)                  | 3              |  |  |
| Erysipelas                         |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Furuncle                           |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Eye infection                      |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Upper respiratory tract infection  |                |  |  |
| subjects affected / exposed        | 2 / 45 (4.44%) |  |  |
| occurrences (all)                  | 2              |  |  |
| Tooth infection                    |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Oral herpes                        |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Nasopharyngitis                    |                |  |  |
| subjects affected / exposed        | 2 / 45 (4.44%) |  |  |
| occurrences (all)                  | 2              |  |  |
| Mucosal infection                  |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 3              |  |  |
| Wound infection                    |                |  |  |
| subjects affected / exposed        | 1 / 45 (2.22%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Urinary tract infection            |                |  |  |
| subjects affected / exposed        | 2 / 45 (4.44%) |  |  |
| occurrences (all)                  | 2              |  |  |
| Metabolism and nutrition disorders |                |  |  |

|                                                                        |                      |  |  |
|------------------------------------------------------------------------|----------------------|--|--|
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 4 / 45 (8.89%)<br>6  |  |  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)        | 1 / 45 (2.22%)<br>1  |  |  |
| Gout<br>subjects affected / exposed<br>occurrences (all)               | 1 / 45 (2.22%)<br>1  |  |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)      | 2 / 45 (4.44%)<br>2  |  |  |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)     | 6 / 45 (13.33%)<br>6 |  |  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)       | 1 / 45 (2.22%)<br>1  |  |  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)      | 1 / 45 (2.22%)<br>1  |  |  |
| Iron overload<br>subjects affected / exposed<br>occurrences (all)      | 1 / 45 (2.22%)<br>1  |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 July 2019     | This amendment: excluded subjects eligible for allogeneic hematopoietic stem cell treatment (ASCT); clarified that any subjects scheduled for ASCT during the study were to be discontinued; aligned updated information available from the sabatolimab (MBG453) Investigator's Brochure to use highly effective forms of contraception for women of child-bearing potential (WOCBP) for up to 150 days for subjects on study treatment that included sabatolimab; clarified that the safety follow-up for subjects on study treatment that included sabatolimab was up to 150 days; safety follow-ups were to be conducted at 30, 90, and 150 days; excluded all forms of hormonal contraception for WOCBP (for consistency, hormonal contraception was excluded from all arms of the study); excluded subjects who could not discontinue drugs that strongly induce or inhibit CYP2C9; added strong inducers or inhibitors of CYP2C9 as prohibited medications, advised caution on the use of moderate inducers or inhibitors; clarified for the safety run-in of crizanlizumab and sabatolimab arms of the study in Part 1 that if 2 subjects experienced a dose-limiting toxicity (DLT) in either arm, then further enrolment into that arm would stop, and the treatment combination would not open in Part 2; clarified that intra-subject dose escalation was not allowed; added additional electrocardiogram (ECG) safety monitoring for any QTc interval prolongation > 60 msec from baseline; added a recommendation to protect skin from solar UV radiation if subjects were on study treatment that contained siremadlin; clarified that the Patient Global Impression of Change (PGIC) patient-reported outcome (PRO) was not required at screening; clarified that urine pregnancy tests would be performed monthly for all pre-menopausal women who were not surgically sterile; added further hypothetical on-study data scenarios to the Bayesian model used to guide dose escalation in Part 1 for siremadlin in combination with ruxolitinib. |
| 17 February 2020 | This amendment: clarified definition of accelerated phase for progression free survival; clarified that subjects who had participated in the CINC424H12201 study could participate in a subsequent part of the study; removed exclusion of subjects treated with hematopoietic colony-stimulating growth factors; excluded subjects who used live vaccines within 30 days of starting any study treatment; added live vaccines as prohibited medication for study treatment arms containing crizanlizumab or sabatolimab; excluded subjects who used systemic steroid therapy and other immunosuppressive drugs (> 10 mg/day prednisone or equivalent) within 14 days prior to first dose of study treatment; added use of systemic steroid therapy as prohibited medication, except for treatment of infusion reaction, treatment of immune-related adverse events, prophylaxis against imaging contrast dye allergy, replacement-dose steroids in the setting of adrenal insufficiency (providing this was ≤ 10 mg/day prednisone or equivalent), or treatment of transient exacerbation of other underlying diseases such as chronic obstructive pulmonary disease requiring treatment for ≤ 3 weeks; excluded subjects who used anticoagulation or antiplatelet therapy within 10 days of prior to first dose of study treatment and subjects who had bleeding events within 6 months prior to first dose of study treatment; updated the prohibition of anticoagulation therapy to allow the use of low molecular weight heparin or direct oral anti-coagulants if used at sub-therapeutic doses; added erythropoietin stimulating agents (ESAs) as prohibited medication; updated the dose modification tables specific to the novel agents to remove any reference to ruxolitinib; allowed subjects in Part 1 to continue on study treatment after the planned 6 cycles if the subject was still deriving clinical benefit; defined "overall safety period."                                                                                              |

|                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 28 April 2020    | This amendment: updated Exclusion Criterion #8 to exclude patients with known history of human immunodeficiency virus (HIV) as an overall positive benefit risk ratio to include HIV patients with the various novel combination treatments could not be determined at that stage. In addition, antiretroviral therapy (ART) regimen including strong CYP3A4 inhibitors could lead to the potential drug-drug interaction of one or more study medications; extended the restrictions on the use of live vaccines until the end of the follow-up period after the last dose of crizanlizumab and sabatolimab, which was within 5 half-lives of the study treatment; guidance was added on the criteria for sabatolimab dose management for dermatological adverse drug reactions (ADRs) and non-immune related toxicities; added guidance that subjects should be monitored carefully for any skin toxicity or mucositis, and that study treatment should be discontinued for any suspected case of Stevens-Johnson syndrome (SJS), or Lyell syndrome/toxic epidermal necrolysis (TEN).                                                                                                                                                                                                                                                                                                                     |
| 25 August 2020   | This amendment: added two novel compounds to Part 1 of the protocol: LTT462, which is a potent, selective, inhibitor of extracellular signal-regulated kinase 1 (ERK1) and extracellular signal regulated kinase 2 (ERK2), and NIS793, which is an anti-transforming growth factor beta (anti-TGFβ) monoclonal antibody (mAb); added additional cycles throughout the protocol, where applicable; increased the number of subjects required for Part 2 from 15 subjects per arm to 25 subjects per arm to ensure the acceptable futility probability for applying the futility rule in multiple arms.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 23 February 2021 | This amendment: updated the study design to allow 1) Part 2 (Selection) to be conducted for each combination treatment once the combination treatment was determined to be safe and tolerable in Part 1, and 2) to allow more than one combination treatment selected in Part 2 to enter Part 3 (Expansion); added an interim analysis per combination treatment after at least 10 subjects completed 24 weeks of study treatment in Part 2 to allow for a seamless transition into Part 3 if an efficacy threshold was reached; reduced the number of pharmacokinetic and pharmacodynamic samples collected, including removal of a few assessment visits in Part 2 and Part 3 of the study; included specific requirements for conducting the study in China, Japan, and USA.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 20 July 2021     | This amendment: updated the eligibility criteria to reduce the time required for patients to be treated with ruxolitinib from "at least 24 weeks" to "at least 12 weeks" prior to first dose of study treatment, and also to reduce the time required for patients to be on a stable prescribed dose of ruxolitinib (no dose adjustments) prior to first dose of study treatment from "≥ 8 weeks" to "≥ 4 weeks"; provided more detailed guidance regarding dose modifications of siremadlin, rineterkib and NIS793 in case of toxicity including to allow patients to continue on study treatment at a reduced dose level for siremadlin or rineterkib or, at a reduced frequency for NIS793 if patients derived clinical benefits as per investigator's judgement; additional precautionary measures have been implemented based on emerging new NIS793-related preclinical safety findings including update of exclusion criteria for impaired cardiac function and addition of cardiac imaging and cardiac enzymes safety assessments during treatment to enhance cardio-vascular mitigation; additional guidance on dose discontinuation for NIS793 in case of Drug-induced liver injury (DILI); removed the collection of bone marrow aspirate for megakaryocyte characterization in all parts of the study; updated the withdrawal of consent language as per the latest Novartis protocol template. |
| 11 January 2022  | This amendment: allowed patients requiring packed red blood cell (PRBC) transfusions at any timepoint prior to first dose of study treatment to participate in all parts of the study; added details on the endpoints definitions to assess the following secondary objectives (i) changes in symptoms of myelofibrosis using the Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 scale and (ii) changes in spleen volume to include pre-defined threshold of improvement; added a new strength of rineterkib to allow additional doses of rineterkib to be tested if ever required; updated exclusion criteria to provide a more comprehensive guidance on the time gap between administration of monoclonal antibody or immunoglobulin-based agent for NIS793, crizanlizumab or sabatolimab arms (within 1 year) and rineterkib or siremadlin arms (within ≤4 weeks of screening or ≤5 half-lives, whichever was shorter); added new biomarkers specific for NIS793 and sabatolimab to assess the impact of TGFβ and TIM-3 inhibition with NIS793 and MBG453 on various immune cells.                                                                                                                                                                                                                                                                                                                  |

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| 05 October 2022  | This amendment reflected the changes in study conduct that were a result of the permanent enrollment halt decision by Novartis. These changes included adding an extension treatment phase and reduction of study assessments to decrease subjects' burden in Part 1. |
| 05 December 2023 | This amendment increased the duration of the extension treatment phase for the remaining patients to a maximum of 21 cycles.                                                                                                                                          |

Notes:

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## 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.

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| Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. |
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Notes: