

**Clinical trial results:****A Phase 2, Prospective Study Of PRM-151 In Subjects With Primary Myelofibrosis (PMF), Post-Polycythemia Vera MF (post-PV MF), Or Post-Essential Thrombocythemia MF (post-ET MF)****Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2015-001718-80 |
| Trial protocol | NL FR DE IT |
| Global end of trial date | 10 July 2020 |

Results information

| | |
|--------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number | v4 |
| This version publication date | 14 November 2021 |
| First version publication date | 16 July 2021 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Updates to endpoints 3 and 4 as per comments received from NIH |

Trial information**Trial identification**

| | |
|-----------------------|---------|
| Sponsor protocol code | BO42355 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01981850 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|------------------------------------------------------|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 July 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 July 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Stage 1: The main objective of this part of the study was to evaluate the efficacy of two different dose schedules of single-agent RO7490677 or RO7490677 in combination with ruxolitinib in participants with PMF, post-PV MF, or post ET-MF.

Stage 2: The main objective of this part of the study was to determine the effect size of three different doses of RO7490677 on the reduction in bone marrow fibrosis by ≥ 1 grade in participants with PMF, post-PV MF, or post ET-MF.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment | 01 October 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Israel: 6 |
| Country: Number of subjects enrolled | United States: 78 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Italy: 9 |
| Country: Number of subjects enrolled | Netherlands: 9 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Worldwide total number of subjects | 124 |
| EEA total number of subjects | 24 |

Notes:

Subjects enrolled per age group

| | |
|-------------------------------------------|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

| | |
|------------------------------------------|----|
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 26 |
| From 65 to 84 years | 95 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

A total of 125 participants were enrolled at sites in 8 different countries.

Pre-assignment

Screening details:

One randomized participant in Stage 2 did not receive the study treatment, bringing the total number of treated participants to 124.

Period 1

| | |
|------------------------------|----------------------------------------|
| Period 1 title | Main Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|-----------------------------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) |

Arm description:

Participants who received no treatment for Myelofibrosis (MF) in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 milligram per kilogram (mg/kg) administered as a 30 minute intravenous (IV) infusion on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles.

| | |
|----------------------------------------|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 milligrams per kilogram (mg/kg) of PRM-151 QW via intravenous (IV) infusion.

| | |
|------------------|---------------------------------------------------------------|
| Arm title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) |
|------------------|---------------------------------------------------------------|

Arm description:

Participants who received no treatment for MF in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles.

| | |
|----------------------------------------|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 Q4W via IV infusion.

| | |
|------------------|------------------------------------------------------------|
| Arm title | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib |
|------------------|------------------------------------------------------------|

Arm description:

Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and

Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles.

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

Dosage and administration details:

Participants who received ruxolitinib continued to take ruxolitinib orally twice a day at the dose at which they entered the study.

| | |
|----------------------------------------|-------------------------------|
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 QW via IV infusion.

| | |
|------------------|------------------------------------------------------------|
| Arm title | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|------------------|------------------------------------------------------------|

Arm description:

Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles.

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

Dosage and administration details:

Participants who received ruxolitinib continued to take ruxolitinib orally twice a day at the dose at which they entered the study.

| | |
|----------------------------------------|-------------------------------|
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 Q4W via IV infusion and daily oral ruxolitinib.

| | |
|------------------|------------------------------------------------|
| Arm title | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
|------------------|------------------------------------------------|

Arm description:

Participants were treated with single agent PRM-151 at a dose of 0.3 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles.

| | |
|----------------------------------------|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 0.3 mg/kg of PRM-151 Q4W via IV infusion.

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Arm title | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
| Arm description: | |
| Participants were treated with single agent PRM-151 at a dose of 3.0 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 3 mg/kg of PRM-151 Q4W via IV infusion.

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| Arm title | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
| Arm description: | |
| Participants were treated with single agent PRM-151 at a dose of 10 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 Q4W via IV infusion.

| Number of subjects in period 1 | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib |
|---------------------------------------|--------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------|
| Started | 8 | 7 | 6 |
| Completed | 5 | 5 | 4 |
| Not completed | 3 | 2 | 2 |
| Consent withdrawn by subject | 1 | - | - |
| Adverse Event | - | - | - |
| Death | 2 | - | - |
| Progressive Disease | - | - | - |
| Various reasons | - | - | 2 |
| Lack of efficacy | - | 2 | - |

| Number of subjects in period 1 | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
|---------------------------------------|---------------------------------------------------------------|---------------------------------------------------|-------------------------------------------------|
| Started | 6 | 33 | 32 |
| Completed | 6 | 20 | 16 |
| Not completed | 0 | 13 | 16 |
| Consent withdrawn by subject | - | 4 | 3 |

| | | | |
|---------------------|---|---|---|
| Adverse Event | - | 6 | 5 |
| Death | - | - | - |
| Progressive Disease | - | - | 6 |
| Various reasons | - | 2 | - |
| Lack of efficacy | - | 1 | 2 |

| Number of subjects in period 1 | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
|--------------------------------|-----------------------------------------------------|
| Started | 32 |
| Completed | 15 |
| Not completed | 17 |
| Consent withdrawn by subject | 3 |
| Adverse Event | 7 |
| Death | - |
| Progressive Disease | 6 |
| Various reasons | 1 |
| Lack of efficacy | - |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Open Label Extension |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | OLE Stage 1: RO7490677 10 mg/kg IV Q4W |

Arm description:

Participants who completed the main phase of treatment moved to the open label extension. They were treated with single agent PRM-151 at a dose of 10 mg/kg administered as an IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle.

| | |
|----------------------------------------|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 Q4W via IV infusion.

| | |
|------------------|------------------------------------------------------|
| Arm title | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib |
|------------------|------------------------------------------------------|

Arm description:

Participants who completed the main phase of treatment moved to the open label extension. They were treated with PRM-151 at a dose of 10 mg/kg administered as an IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle.

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

| | |
|----------------------------------------|-------------------------------|
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 Q4W via IV infusion.

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

Dosage and administration details:

Participants who received ruxolitinib continued to take ruxolitinib orally twice a day at the dose at which they entered the study.

| | |
|------------------|----------------------------------------|
| Arm title | OLE Stage 2: RO7490677 10 mg/kg IV Q4W |
|------------------|----------------------------------------|

Arm description:

Participants who completed 9 cycles of the originally assigned treatment could switch to the open label extension. Participants enrolled received PRM-151 at a dose of 10mg/kg Q4W on days 1, 3, and 5 of first cycle of the open label phase and Day 1 of each subsequent 28 day cycle.

| | |
|----------------------------------------|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PRM-151 |
| Investigational medicinal product code | |
| Other name | recombinant human pentraxin-2 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants were administered 10 mg/kg of PRM-151 Q4W via IV infusion.

| Number of subjects in period 2^[1] | OLE Stage 1: RO7490677 10 mg/kg IV Q4W | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib | OLE Stage 2: RO7490677 10 mg/kg IV Q4W |
|-----------------------------------------------------|----------------------------------------------|---------------------------------------------------------------|----------------------------------------------|
| Started | 13 | 5 | 48 |
| Completed | 1 | 0 | 0 |
| Not completed | 12 | 5 | 48 |
| Consent withdrawn by subject | - | - | 8 |
| Adverse Event | 2 | 1 | 8 |
| Progressive Disease | 3 | 2 | 9 |
| Various reasons | 3 | 1 | 3 |
| Lost to follow-up | - | - | 1 |
| Lack of efficacy | 4 | 1 | 19 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the Main Phase entered the OLE.

Baseline characteristics

Reporting groups

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) |
| Reporting group description: Participants who received no treatment for Myelofibrosis (MF) in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 milligram per kilogram (mg/kg) administered as a 30 minute intravenous (IV) infusion on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) |
| Reporting group description: Participants who received no treatment for MF in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib |
| Reporting group description: Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
| Reporting group description: Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
| Reporting group description: Participants were treated with single agent PRM-151 at a dose of 0.3 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Reporting group title | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
| Reporting group description: Participants were treated with single agent PRM-151 at a dose of 3.0 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Reporting group title | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
| Reporting group description: Participants were treated with single agent PRM-151 at a dose of 10 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |

| Reporting group values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib |
|----------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|
| Number of subjects | 8 | 7 | 6 |
| Age Categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |

| | | | |
|-------------------------------------------|--------|-------|-------|
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 4 | 1 | 1 |
| From 65-84 years | 3 | 6 | 5 |
| 85 years and over | 1 | 0 | 0 |
| Age Continuous | | | |
| Participants in the Main Phase | | | |
| Units: years | | | |
| arithmetic mean | 64.3 | 70.7 | 66.0 |
| standard deviation | ± 11.4 | ± 6.3 | ± 7.3 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 2 | 3 |
| Male | 3 | 5 | 3 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 1 |
| Asian | 0 | 0 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 0 | 1 |
| White | 7 | 7 | 3 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |

| Reporting group values | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
|-------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------|----------------------------------------------------|
| Number of subjects | 6 | 33 | 32 |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 3 | 6 | 5 |
| From 65-84 years | 3 | 27 | 27 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Participants in the Main Phase | | | |
| Units: years | | | |
| arithmetic mean | 66.2 | 70.6 | 70.2 |
| standard deviation | ± 8.6 | ± 7.1 | ± 6.5 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 16 | 8 |
| Male | 1 | 17 | 24 |

| | | | |
|-------------------------------------------|---|----|----|
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 1 |
| White | 6 | 33 | 29 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 1 |

| | | | |
|-------------------------------------------------------|-----------------------------------------------------|-------|--|
| Reporting group values | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | Total | |
| Number of subjects | 32 | 124 | |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 6 | 26 | |
| From 65-84 years | 24 | 95 | |
| 85 years and over | 2 | 3 | |
| Age Continuous | | | |
| Participants in the Main Phase | | | |
| Units: years | | | |
| arithmetic mean | 69.4 | | |
| standard deviation | ± 8.9 | - | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 11 | 50 | |
| Male | 21 | 74 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | |
| Asian | 2 | 4 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 3 | |
| White | 29 | 114 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 1 | 2 | |

End points

End points reporting groups

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) |
| Reporting group description: Participants who received no treatment for Myelofibrosis (MF) in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 milligram per kilogram (mg/kg) administered as a 30 minute intravenous (IV) infusion on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) |
| Reporting group description: Participants who received no treatment for MF in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib |
| Reporting group description: Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
| Reporting group description: Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles. | |
| Reporting group title | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
| Reporting group description: Participants were treated with single agent PRM-151 at a dose of 0.3 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Reporting group title | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
| Reporting group description: Participants were treated with single agent PRM-151 at a dose of 3.0 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Reporting group title | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
| Reporting group description: Participants were treated with single agent PRM-151 at a dose of 10 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles. | |
| Reporting group title | OLE Stage 1: RO7490677 10 mg/kg IV Q4W |
| Reporting group description: Participants who completed the main phase of treatment moved to the open label extension. They were treated with single agent PRM-151 at a dose of 10 mg/kg administered as an IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle. | |
| Reporting group title | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib |
| Reporting group description: Participants who completed the main phase of treatment moved to the open label extension. They were treated with PRM-151 at a dose of 10 mg/kg administered as an IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle. | |
| Reporting group title | OLE Stage 2: RO7490677 10 mg/kg IV Q4W |
| Reporting group description: Participants who completed 9 cycles of the originally assigned treatment could switch to the open label extension. Participants enrolled received PRM-151 at a dose of 10mg/kg Q4W on days 1, 3, and 5 of | |

first cycle of the open label phase and Day 1 of each subsequent 28 day cycle.

| | |
|----------------------------|----------------------------------------------|
| Subject analysis set title | Main Phase Stage 1: RO7490677 10 mg/kg IV QW |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles.

| | |
|----------------------------|-----------------------------------------------------|
| Subject analysis set title | Main Phase + OLE Stage 1: RO7490677 10 mg/kg IV Q4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants who received no treatment for MF in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles (main phase) and on Days 1, 3, and 5 of Cycle 7 and Day 1 of each subsequent 28 day cycle for 83 cycles (OLE).

| | |
|----------------------------|----------------------------------------------------------|
| Subject analysis set title | Main Phase Stage 1: RO7490677 10 mg/kg IV QW+Ruxolitinib |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants who received no treatment for Myelofibrosis (MF) in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 milligram per kilogram (mg/kg) administered as a 30 minute intravenous (IV) infusion on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles.

| | |
|----------------------------|--------------------------------------------------------------|
| Subject analysis set title | Main Phase+OLE Stg. 1: RO7490677 10 mg/kg IV Q4W+Ruxolitinib |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles (main phase) and on Days 1, 3, and 5 of Cycle 7 and Day 1 of each subsequent 28 day cycle for 83 cycles (OLE).

| | |
|----------------------------|------------------------------------------------|
| Subject analysis set title | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants were treated with single agent PRM-151 at a dose of 0.3 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles.

| | |
|----------------------------|----------------------------------------------|
| Subject analysis set title | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants were treated with single agent PRM-151 at a dose of 3.0 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles.

| | |
|----------------------------|-----------------------------------------------------|
| Subject analysis set title | Main Phase + OLE Stage 2: RO7490677 10 mg/kg IV Q4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants enrolled received PRM-151 at a dose of 10mg/kg Q4W on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for 9 cycles (main phase) and on Days 1, 3, and 5 of Cycle 10 and Day 1 of each subsequent 28 day cycle for 51 cycles (OLE).

Primary: Stage 1 Main Phase: Overall Response Rate (ORR)

| | |
|-----------------|-------------------------------------------------------------------|
| End point title | Stage 1 Main Phase: Overall Response Rate (ORR) ^{[1][2]} |
|-----------------|-------------------------------------------------------------------|

End point description:

ORR was defined as the percent of participants with a response according to the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) criteria. This was defined as those participants who achieved clinical improvement (CI), partial remission (PR), or complete remission (CR) at a post-baseline assessment of treatment response OR had at least stable disease (SD) for three

consecutive end-of-cycle response assessments (e.g. Day 1 of the subsequent cycle) in conjunction with improvement in the bone marrow fibrosis score relative to baseline by at least one grade at any time point during the period of stable disease. The all treated population included all participants who received at least one dose of RO7490667.

| | |
|-----------------------------------------------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Up until and including completion of 6 cycles. Each cycle is 28 days. | |

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: For stage 1, the hypothesis test was performed separately in each of the 4 treatment groups and overall, each at 5% significance level (one-sided; statistical significance was concluded if the lower bound of the 2 sided 90% CI was above 10%).

[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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 90%) | 37.5 (11.11 to 71.08) | 14.3 (0.73 to 52.07) | 33.3 (6.28 to 72.87) | 50.0 (15.32 to 84.68) |

Statistical analyses

No statistical analyses for this end point

Primary: Stage 2 Main Phase: Bone Marrow Response Rate (BMRR)

| | |
|-----------------|------------------------------------------------------------------------|
| End point title | Stage 2 Main Phase: Bone Marrow Response Rate (BMRR) ^{[3][4]} |
|-----------------|------------------------------------------------------------------------|

End point description:

Response rate was defined as the percent of participants with a reduction in bone marrow fibrosis by at least one grade according to World Health Organization (WHO) criteria from baseline to any time during the study. This was determined by a central adjudication panel of expert hematopathologists, blinded to participant, treatment, and time of biopsy. The all treated population included all participants randomized and who received at least one administration of the drug.

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

End point timeframe:

Up until and including completion of 9 cycles. Each cycle is 28 days.

Notes:

[3] - 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: For stage 2, two pairwise comparisons (3 mg/kg vs 0.3 mg/kg and 10 mg/kg vs 0.3 mg/kg) were computed with aim to demonstrate superiority and therefore, used an adjusted two-sided level of significance of 0.025. The third comparison (10 mg/kg vs 3mg/kg) was not expected to have enough power to demonstrate any difference with the planned sample size. This comparison was considered exploratory and was conducted using an unadjusted two-sided 0.05 level of significance.

[4] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| | | | | |
|-----------------------------------|---------------------------------------------------------|----------------------------------------------------|-----------------------------------------------------|--|
| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 30.3 (14.62 to 45.98) | 31.3 (15.19 to 47.31) | 25.0 (10.00 to 40.00) | |

Statistical analyses

No statistical analyses for this end point

Primary: Stage 1 Main + Open-Label Extension (OLE): ORR

| | |
|-----------------|------------------------------------------------------------------|
| End point title | Stage 1 Main + Open-Label Extension (OLE): ORR ^{[5][6]} |
|-----------------|------------------------------------------------------------------|

End point description:

ORR was defined as the percent of participants with a response according to the IWG-MRT criteria. This was defined as those participants who achieved CI, PR, or CR at a post-baseline assessment of treatment response OR had at least SD for three consecutive end-of-cycle response assessments (e.g. Day 1 of the subsequent cycle) in conjunction with improvement in the bone marrow fibrosis score relative to baseline by at least one grade at any time point during the period of stable disease. Participants who achieved a clinical benefit in the main phase had the opportunity to remain on treatment. The determination of ORR in the main phase is outlined in the subject analysis set description. Participants who didn't achieve a benefit had the opportunity to switch to a different dosing schedule in the OLE phase. The determination of ORR in the OLE phase is outlined in the subject analysis set description.

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

End point timeframe:

From cycle 1 day 1 up until cycle 6, day 29 (Main Phase). From cycle 7 day 1 up until study discontinuation or study termination, up to 83 cycles (OLE). Each cycle is 28 days.

Notes:

[5] - 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: For stage 1, the hypothesis test was performed separately in each of the 4 treatment groups and overall, each at 5% significance level (one-sided; statistical significance was concluded if the lower bound of the 2 sided 90% CI was above 10%).

[6] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| | | | | |
|-----------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------|--------------------------------------------------------------|-----------------------------------------------------------------------------|
| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase + OLE Stage 1: RO7490677 10 mg/kg IV Q4W | Main Phase+OLE Stg. 1: RO7490677 10 mg/kg IV Q4W+Ruxolitinib |
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 8 | 6 | 7 | 6 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 90%) | 50.0 (19.29 to 80.71) | 50.0 (15.32 to 84.68) | 71.4 (34.13 to 94.66) | 66.7 (27.13 to 93.72) |

Statistical analyses

No statistical analyses for this end point

Primary: Stage 2 Main + Open-Label Extension (OLE): BMRR

| | |
|-----------------|-------------------------------------------------------------------|
| End point title | Stage 2 Main + Open-Label Extension (OLE): BMRR ^{[7][8]} |
|-----------------|-------------------------------------------------------------------|

End point description:

Defined as the percent of participants with a reduction in bone marrow fibrosis score by at least one grade according to WHO criteria at any time during the study. As determined by a central adjudication panel of expert hematopathologists, blinded to participant, treatment, and time of biopsy. Participants in the main phase had the opportunity to remain on treatment (as outlined in the subject analysis set description). Participants also had the option to switch to the OLE phase after completing 9 cycles of the originally assigned treatment and receive PRM-151 10 mg/kg/Q4W (as outlined in the subject analysis set description).

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

End point timeframe:

From cycle 1 day 1 up until cycle 9 day 29 (main phase). From cycle 10 day 1 up until study discontinuation or study termination, up to 51 cycles (OLE). Each cycle is 28 days.

Notes:

[7] - 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: For stage 2, two pairwise comparisons (3 mg/kg vs 0.3 mg/kg and 10 mg/kg vs 0.3 mg/kg) were computed with aim to demonstrate superiority and therefore, used an adjusted two-sided level of significance of 0.025. The third comparison (10 mg/kg vs 3mg/kg) was not expected to have enough power to demonstrate any difference with the planned sample size. This comparison was considered exploratory and was conducted using an unadjusted two-sided 0.05 level of significance.

[8] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase + OLE Stage 2: RO7490677 10 mg/kg IV Q4W | |
|-----------------------------------|------------------------------------------------|----------------------------------------------|-----------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 30.3 (14.62 to 45.98) | 34.4 (17.92 to 50.83) | 25.0 (10.00 to 40.00) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1 Main Phase: BMRR

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| End point title | Stage 1 Main Phase: BMRR ^[9] |
| End point description: Bone marrow response was defined as a reduction in bone marrow fibrosis score by at least one grade from baseline at anytime during the study. The all treated population included all participants who received at least one dose of RO7490667. | |
| End point type | Secondary |
| End point timeframe: Baseline, Weeks 12 and 24 | |

Notes:

[9] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 37.5 (3.95 to 71.05) | 14.3 (0.00 to 40.21) | 16.7 (0.00 to 46.49) | 50.0 (9.99 to 90.01) |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1 Main Phase: Modified Myeloproliferative Neoplasms Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) Changes

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Stage 1 Main Phase: Modified Myeloproliferative Neoplasms Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) Changes ^[10] |
| End point description: The MPN-SAF TSS total symptom score was the sum of the following 10 items: Filling up quickly when you eat (early satiety), abdominal discomfort, inactivity, Problems with concentration, Worst fatigue, Night sweats, Itching, Bone pain, Fever and Unintentional weight loss last 6 months. The MPN-SAF Total Symptom Score had a possible range of 0 to 100, where a lower score was more favorable. The values reported are the change from baseline scores. The all treated population included all participants who received at least one dose of RO7490667. | |
| End point type | Secondary |
| End point timeframe: Baseline, beginning of each cycle (Cycle 2 onward). Each cycle is 28 days. | |

Notes:

[10] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|--------------------------------------|--------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 8,7,6,6) | 23.1 (± 19.1) | 16.9 (± 7.2) | 26.8 (± 17.1) | 15.3 (± 10.4) |
| Cycle(C) 2 Day(D) 1 (n= 7,6,6,6) | -5.3 (± 12.6) | 5.7 (± 11.8) | 0.5 (± 8.8) | -2.0 (± 5.0) |
| C3D1 (n= 7,7,6,5) | -9.1 (± 10.9) | 1.9 (± 5.3) | -2.7 (± 14.8) | 4.2 (± 8.0) |
| C4D1 (n= 7,7,6,6) | -8.7 (± 10.7) | 1.0 (± 8.0) | -7.5 (± 6.0) | 5.7 (± 20.9) |
| C5D1 (n= 5,7,6,6) | -13.2 (± 13.2) | 2.6 (± 6.9) | -6.7 (± 10.6) | 1.5 (± 13.6) |
| C6D1 (n= 5,5,5,6) | -12.2 (± 9.5) | -0.8 (± 8.3) | -5.4 (± 6.2) | 4.3 (± 11.5) |
| C6D29 (n= 5,5,4,4) | -15.0 (± 13.7) | -2.2 (± 5.3) | -5.3 (± 4.6) | 2.3 (± 8.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: BMRR

| | |
|-----------------|------------------------------------------|
| End point title | Stage 2 Main Phase: BMRR ^[11] |
|-----------------|------------------------------------------|

End point description:

Response rate was defined as the percent of participants with a reduction in bone marrow fibrosis by at least one grade according to World Health Organization (WHO) criteria at any time during the study. This was determined by a central adjudication panel of expert hematopathologists, blinded to participant, treatment, and time of biopsy. The all treated population included all participants randomized and who received at least one administration of the drug.

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

End point timeframe:

Up until and including completion of 9 cycles. Each cycle is 28 days.

Notes:

[11] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|-----------------------------------|---------------------------------------------------|-------------------------------------------------|--------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 30.3 (14.62 to 45.98) | 31.3 (15.19 to 47.31) | 25.0 (10.0 to 40.00) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: BMRR - Reduction of Bone Marrow Fibrosis by Visit

| | |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Stage 2 Main Phase: BMRR - Reduction of Bone Marrow Fibrosis by Visit ^[12] |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

Reduction in bone marrow fibrosis score: Reduction of at least one grade from baseline. Bone marrow fibrosis grades according to WHO criteria (as determined by central adjudication). The all treated population included all participants randomized and who received at least one administration of the drug.

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

End point timeframe:

Day 1 on Cycles 4, 7, 10 and Cycle 9 Day 29. Each cycle is 28 days.

Notes:

[12] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|-----------------------------------|------------------------------------------------|----------------------------------------------|-----------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Cycle(C) 4 Day(D) 1 (n=28,25,26) | 10.7 | 24.0 | 19.2 | |
| C7D1 (n=21,17,19) | 23.8 | 11.8 | 10.5 | |
| C9D29/C10D1 (n=20,14,15) | 30.0 | 21.4 | 13.3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: Duration of Bone Marrow Improvement

| | |
|-----------------|-------------------------------------------------------------------------|
| End point title | Stage 2 Main Phase: Duration of Bone Marrow Improvement ^[13] |
|-----------------|-------------------------------------------------------------------------|

End point description:

Duration of response was defined as time from first decrease from baseline ≥ 1 grade to time of return to baseline levels. The all treated population included all participants randomized and who received at least one administration of the drug. 9999999 = participants who had bone marrow improvement but did not return to baseline levels at the end of main phase were censored at their last bone marrow assessment in the main phase (the last timepoint in the main phase at which the improvement was still observed).

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

End point timeframe:

From first decrease from baseline of one grade to time of return to baseline levels, up to cycle 9 of 28-day cycles.

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|----------------------------------|------------------------------------------------|----------------------------------------------|-----------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Weeks | | | | |
| median (confidence interval 95%) | 9999999 (12.0 to 9999999) | 12.0 (12.0 to 9999999) | 12.1 (11.4 to 13.0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: Hemoglobin Improvement

| | |
|-----------------|------------------------------------------------------------|
| End point title | Stage 2 Main Phase: Hemoglobin Improvement ^[14] |
|-----------------|------------------------------------------------------------|

End point description:

Hemoglobin improvement was measured by the percent of participants with: Red cell transfusion independence (no transfusions for ≥ 12 consecutive weeks) OR 50% reduction in red blood cell (RBC) transfusions for ≥ 12 consecutive weeks OR percent of participants with ≥ 10 g/L and ≥ 20 g/L increase in hemoglobin for ≥ 12 consecutive weeks without transfusions (outcome parameter assessed was dependent on baseline hemoglobin/transfusion status). The all treated population included all participants randomized and who received at least one administration of the drug.

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

End point timeframe:

Up until and including completion of 9 cycles. Each cycle is 28 days.

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|-----------------------------------|------------------------------------------------|----------------------------------------------|-----------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 15.2 | 15.6 | 6.3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: Platelet Improvement

End point title Stage 2 Main Phase: Platelet Improvement^[15]

End point description:

Platelet improvement was measured by the percent of participants with: Platelet transfusion independence (no transfusions for ≥ 12 consecutive weeks) OR 50% reduction in platelets transfusions for ≥ 12 consecutive weeks OR doubling of baseline platelet count for ≥ 12 consecutive weeks without platelet transfusions OR platelet count $> 50 \times 10^9/L$ for ≥ 12 consecutive weeks without platelet transfusions OR doubling of baseline platelet count for ≥ 12 consecutive weeks without platelet transfusions OR platelet count $> 25 \times 10^9/L$ for ≥ 12 consecutive weeks without platelet transfusions (outcome parameter assessed is dependent on baseline platelet status). The all treated population included all participants randomized and who received at least one administration of the drug.

End point type Secondary

End point timeframe:

Up until and including completion of 9 cycles. Each cycle is 28 days.

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|-----------------------------------|------------------------------------------------|----------------------------------------------|-----------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 27.3 | 34.4 | 37.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: Symptom Improvement

End point title Stage 2 Main Phase: Symptom Improvement^[16]

End point description:

Symptom improvement was assessed as the percent of participants with 50% reduction in MPN-SAF TSS from baseline over time. The MPN-SAF TSS total symptom score was the sum of the following 10 items: Filling up quickly when you eat (early satiety), abdominal discomfort, inactivity, Problems with concentration, Worst fatigue, Night sweats, Itching, Bone pain, Fever and Unintentional weight loss last 6 months. The MPN-SAF Total Symptom Score had a possible range of 0 to 100, where a lower score was more favorable. The all treated population included all participants randomized and who received at least one administration of the drug.

End point type Secondary

End point timeframe:

Up until and including completion of 9 cycles. Each cycle is 28 days.

Notes:

[16] - 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: Data is being provided for each stage of this study rather than all arms in the baseline

period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|------------------------------------|------------------------------------------------|----------------------------------------------|-----------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Cycle(C) 2 Day(D) 1 (n=31, 31, 29) | 16.1 | 6.5 | 3.4 | |
| C3D1 (n=30, 29, 28) | 20.0 | 10.3 | 7.1 | |
| C4D1 (n=28, 29, 28) | 10.7 | 13.8 | 7.1 | |
| C5D1 (n=24, 25, 25) | 20.8 | 8.0 | 4.0 | |
| C6D1 (n=23, 21, 25) | 34.8 | 14.3 | 12.0 | |
| C7D1 (n=21, 18, 20) | 38.1 | 27.8 | 0 | |
| C8D1 (n=20, 18, 19) | 25.0 | 16.7 | 0 | |
| C9D1 (n=21, 17, 17) | 23.8 | 17.6 | 5.9 | |
| C9D29/C10D1 (n=20, 16, 13) | 25.0 | 12.5 | 0 | |
| End of Main Study (n=6, 7, 7) | 16.7 | 0 | 14.3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2 Main Phase: Percentage of Participants with Complete Response (CR), Partial Response (PR), Clinical Improvement (CI), Stable Disease (SD), and Progressive Disease (PD) According to IWG-MRT Criteria

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Stage 2 Main Phase: Percentage of Participants with Complete Response (CR), Partial Response (PR), Clinical Improvement (CI), Stable Disease (SD), and Progressive Disease (PD) According to IWG-MRT Criteria ^[17] |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Best Overall Response: (CR Response, PR, CI), SD and PD according to the IWG-MRT Criteria. The all treated population included all participants randomized and who received at least one administration of the drug.

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

End point timeframe:

Up until and including completion of 9 cycles. Each cycle is 28 days.

Notes:

[17] - 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | |
|-----------------------------------|---------------------------------------------------------|----------------------------------------------------|-----------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 32 | 32 | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| CR | 0 | 0 | 0 | |
| PR | 0 | 0 | 0 | |
| CI | 24.2 | 18.8 | 6.3 | |
| SD | 60.6 | 65.6 | 81.3 | |
| PD | 9.1 | 9.4 | 12.5 | |
| Not evaluable | 6.1 | 6.3 | 0 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Maximum Drug Concentration (Cmax)

| | |
|-----------------|-----------------------------------------------------------------------|
| End point title | Stage 1 Main Phase: Maximum Drug Concentration (Cmax) ^[18] |
|-----------------|-----------------------------------------------------------------------|

End point description:

Cmax is the maximum observed RO7490677 plasma concentration. The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999 = no samples were analyzed.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 28 days

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Micrograms per Milliliter (ug/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=7,7,6,6) | 133 (± 48.4) | 113 (± 28.1) | 164 (± 23.9) | 112 (± 90.4) |
| C1D15 (n=7,0,6,0) | 127 (± 31.9) | 9999999 (± 9999999) | 126 (± 27.5) | 9999999 (± 9999999) |
| C2D1 (n=7,7,6,6) | 107 (± 26.9) | 110 (± 20.9) | 149 (± 29.1) | 130 (± 80.2) |
| C6D1 (n=5,5,5,6) | 142 (± 70.0) | 111 (± 28.0) | 136 (± 34.1) | 142 (± 27.4) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Time to Maximum Concentration (Tmax)

| | |
|-----------------|---------------------------------------------------|
| End point title | Stage 1 Main Phase: Time to Maximum Concentration |
|-----------------|---------------------------------------------------|

End point description:

Time at which the maximum plasma concentration was observed. The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999 = no samples were analyzed.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 28 days

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Hour (hr) | | | | |
| median (full range (min-max)) | | | | |
| C1D1 (n=7,7,6,6) | 1.12 (1.00 to 2.00) | 1.10 (1.00 to 2.08) | 1.14 (1.00 to 2.25) | 1.13 (1.00 to 5.00) |
| C1D15 (n=7,0,6,0) | 1.13 (1.03 to 1.80) | 9999999 (9999999 to 9999999) | 1.65 (1.02 to 2.50) | 9999999 (9999999 to 9999999) |
| C2D1 (n=7,7,6,6) | 1.10 (1.00 to 3.17) | 1.08 (1.03 to 1.08) | 1.05 (1.00 to 1.32) | 1.44 (1.00 to 9.00) |
| C6D1 (n=5,5,5,6) | 2.00 (1.03 to 5.20) | 1.07 (1.00 to 2.03) | 1.17 (1.05 to 5.00) | 1.01 (1.00 to 1.08) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Area Under the Curve up to the Last Measurable Concentration (AUC0-last)

| | |
|-----------------|---------------------------------------------------------|
| End point title | Stage 1 Main Phase: Area Under the Curve up to the Last |
|-----------------|---------------------------------------------------------|

End point description:

Area under the plasma concentration time curve from time 0 to time of last measurable plasma concentration. The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999 = no samples were analyzed.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 28 days

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: ug*hour/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=7,7,6,6) | 1810 (± 72.0) | 1690 (± 26.1) | 2590 (± 28.7) | 1500 (± 158.3) |
| C1D15 (n=7,0,6,0) | 1460 (± 142.0) | 9999999 (± 9999999) | 2590 (± 187.6) | 9999999 (± 9999999) |
| C2D1 (n=7,7,6,6) | 127.3 (± 904) | 504 (± 84.7) | 2990 (± 92.0) | 663 (± 79.5) |
| C6D1 (n=5,5,5,6) | 698 (± 63.0) | 570 (± 44.8) | 764 (± 28.9) | 703 (± 33.8) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Area Under the Concentration-Time Curve Extrapolated to Infinity (AUC0-inf)

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------|
| End point title | Stage 1 Main Phase: Area Under the Concentration-Time Curve Extrapolated to Infinity (AUC0-inf) ^[21] |
|-----------------|-----------------------------------------------------------------------------------------------------------------|

End point description:

Area under the plasma concentration-time curve from 0-time extrapolated to infinity. The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999= no samples were analyzed (for C1D15), the geometric mean and geometric coefficient of variation weren't calculated due to terminal phase calculation criteria not being met and the data could not be calculated from data for a single participant.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 28 days

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: ug*hour/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=3,7,5,3) | 2830 (± 12.9) | 2050 (± 29.5) | 2970 (± 34.9) | 3130 (± 8.6) |
| C1D15 (n=4,0,4,0) | 3450 (± 2.8) | 9999999 (± 9999999) | 6060 (± 23.2) | 9999999 (± 9999999) |
| C2D1 (n=3,0,5,0) | 2170 (± 170.9) | 9999999 (± 9999999) | 4230 (± 34.8) | 9999999 (± 9999999) |
| C6D1 (n=0,0,1,0) | 9999999 (± 9999999) | 9999999 (± 9999999) | 819 (± 9999999) | 9999999 (± 9999999) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Terminal Elimination Half-Life (T1/2)

| | |
|-----------------|---------------------------------------------------------------------------|
| End point title | Stage 1 Main Phase: Terminal Elimination Half-Life (T1/2) ^[22] |
|-----------------|---------------------------------------------------------------------------|

End point description:

Apparent terminal elimination half-life of RO7490677. The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999= no samples were analyzed (for C1D15), the geometric mean and geometric coefficient of variation weren't calculated due to terminal phase calculation criteria not being met and the data could not be calculated from data for a single participant.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 28 days

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: hr | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=3,7,5,3) | 14.7 (± 19.2) | 17.2 (± 23.7) | 16.8 (± 17.7) | 18.4 (± 7.9) |
| C1D15 (n=4,0,4,0) | 31.2 (± 45.0) | 9999999 (± 9999999) | 40.4 (± 12.6) | 9999999 (± 9999999) |

| | | | | |
|------------------|---------------------|---------------------|------------------|---------------------|
| C2D1 (n=3,0,5,0) | 18.0 (± 220.6) | 9999999 (± 9999999) | 30.0 (± 48.6) | 9999999 (± 9999999) |
| C6D1 (n=0,0,1,0) | 9999999 (± 9999999) | 9999999 (± 9999999) | 1.95 (± 9999999) | 9999999 (± 9999999) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Clearance (CL)

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| End point title | Stage 1 Main Phase: Clearance (CL) ^[23] |
| End point description: The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999= no samples were analyzed (for C1D15), the geometric mean and geometric coefficient of variation weren't calculated due to terminal phase calculation criteria not being met and the data could not be calculated from data for a single participant. | |
| End point type | Other pre-specified |
| End point timeframe: Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 28 days | |

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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Litres per hour (L/hr) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=3,7,5,3) | 0.258 (± 9.0) | 0.362 (± 31.5) | 0.269 (± 32.9) | 0.233 (± 33.3) |
| C1D15 (n=4,0,4,0) | 0.233 (± 24.9) | 9999999 (± 9999999) | 0.147 (± 35.0) | 9999999 (± 9999999) |
| C2D1 (n=3,0,5,0) | 0.382 (± 229.9) | 9999999 (± 9999999) | 0.189 (± 55.5) | 9999999 (± 9999999) |
| C6D1 (n=0,0,1,0) | 9999999 (± 9999999) | 9999999 (± 9999999) | 1.42 (± 9999999) | 9999999 (± 9999999) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Stage 1 Main Phase: Volume of Distribution (Vd)

| | |
|-----------------|-----------------------------------------------------------------|
| End point title | Stage 1 Main Phase: Volume of Distribution (Vd) ^[24] |
|-----------------|-----------------------------------------------------------------|

End point description:

The PK population included all participants who received at least one dose of rhPTX-2 and had at least one post-dose total PTX-2 concentration result. 9999999= no samples were analyzed (for C1D15), the geometric mean and geometric coefficient of variation weren't calculated due to terminal phase calculation criteria not being met and the data could not be calculated from data for a single participant.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Pre-dose on Cycles(C) 1, 2 and 6, Day(D) 1 and C1 D15. Each cycle is 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: Data is being provided for each stage of this study rather than all arms in the baseline period at once.

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 7 | 6 | 6 |
| Units: Litres (L) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=3,7,5,3) | 5.47 (± 10.9) | 9.00 (± 28.8) | 6.52 (± 2.64) | 6.17 (± 38.9) |
| C1D15 (n=4,0,4,0) | 10.5 (± 62.4) | 9999999 (± 9999999) | 8.57 (± 47.6) | 9999999 (± 9999999) |
| C2D1 (n=3,0,5,0) | 9.93 (± 63.0) | 9999999 (± 9999999) | 8.18 (± 24.5) | 9999999 (± 9999999) |
| C6D1 (n=0,0,1,0) | 9999999 (± 9999999) | 9999999 (± 9999999) | 4.01 (± 9999999) | 9999999 (± 9999999) |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with Adverse Events (AEs) and Infusion Related Reactions (IRRs)

| | |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants with Adverse Events (AEs) and Infusion Related Reactions (IRRs) |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

An AE was defined as any noxious, pathologic, or unintended change in anatomical, physiologic, or metabolic function as indicated by physical signs, symptoms, or laboratory changes occurring in any phase of a clinical study, whether or not considered investigational product-related. Pre-existing conditions which worsened during the study were also considered as adverse events. IRRs were considered to be Adverse Events of Special Interest (AESI). Grading was completed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.0. The safety population included all participants who received at least one dose of study drug.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline up until 6.75 years

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | OLE Stage 1: RO7490677 10 mg/kg IV Q4W | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib |
|-----------------------------------|-----------------------------------------------------------|----------------------------------------|---------------------------------------------------------------|------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 13 | 7 | 5 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| AEs | 100 | 92.3 | 85.7 | 100 |
| IRRs | 0 | 7.7 | 0 | 20.0 |

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | OLE Stage 2: RO7490677 10 mg/kg IV Q4W | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
|-----------------------------------|------------------------------------------------------------|----------------------------------------|------------------------------------------------------------|------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 48 | 6 | 33 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| AEs | 100 | 89.6 | 100 | 100 |
| IRRs | 0 | 2.1 | 16.7 | 3.0 |

| End point values | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | | |
|-----------------------------------|----------------------------------------------|-----------------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 32 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| AEs | 100 | 100 | | |
| IRRs | 3.1 | 6.3 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with Serious Adverse Events (SAEs) and AEs Leading to Study Drug Discontinuation

| | |
|-----------------|---------------------------------------------------------------|
| End point title | Percentage of Participants with Serious Adverse Events (SAEs) |
|-----------------|---------------------------------------------------------------|

End point description:

An SAE was defined as any AE that occurred at any dose the resulted in death; was life-threatening; required hospitalization or prolongation of existing hospitalizations; a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; a congenital anomaly or birth defect. An AE was defined as any noxious, pathologic, or unintended change in anatomical, physiologic, or metabolic function as indicated by physical signs, symptoms, or laboratory changes occurring in any phase of a clinical study, whether or not considered investigational product-related. Pre-existing conditions which worsened during the study were also considered as adverse events. Grading was completed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.0. The safety population included all participants who received at least one dose of study drug.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline up until 6.75 years

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | OLE Stage 1: RO7490677 10 mg/kg IV Q4W | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib |
|-----------------------------------|-----------------------------------------------------------|----------------------------------------|---------------------------------------------------------------|------------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 13 | 7 | 5 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| SAEs | 25.0 | 7.7 | 0 | 0 |
| AEs | 25.0 | 30.8 | 0 | 0 |

| End point values | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | OLE Stage 2: RO7490677 10 mg/kg IV Q4W | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
|-----------------------------------|------------------------------------------------------------|----------------------------------------|------------------------------------------------------------|------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 48 | 6 | 33 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| SAEs | 0 | 22.9 | 0 | 15.2 |
| AEs | 0 | 27.1 | 0 | 21.2 |

| End point values | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W | | |
|-----------------------------------|----------------------------------------------|-----------------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 32 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |

| | | | | |
|------|------|------|--|--|
| SAEs | 15.6 | 28.1 | | |
| AEs | 34.4 | 37.5 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up until 6.75 years

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) were defined as any AE that occurred after the administration of any amount of the study drug, or any event that was present at baseline.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------------------------------------------------|
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib |
|-----------------------|------------------------------------------------------------|

Reporting group description:

Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles.

| | |
|-----------------------|------------------------------------------------|
| Reporting group title | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W |
|-----------------------|------------------------------------------------|

Reporting group description:

Participants were treated with single agent PRM-151 at a dose of 0.3 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles.

| | |
|-----------------------|-----------------------------------------------|
| Reporting group title | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
|-----------------------|-----------------------------------------------|

Reporting group description:

Participants were treated with single agent PRM-151 at a dose of 10 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles.

| | |
|-----------------------|-----------------------------------------------------------|
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) |
|-----------------------|-----------------------------------------------------------|

Reporting group description:

Participants who received no treatment for Myelofibrosis (MF) in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 milligram per kilogram (mg/kg) administered as a 30 minute intravenous (IV) infusion on Days 1, 3, 5, 8, 15, and 22 of Cycle 1 and Days 1, 8, 15 and 22 of each subsequent 28 day cycle for six cycles.

| | |
|-----------------------|----------------------------------------|
| Reporting group title | OLE Stage 2: RO7490677 10 mg/kg IV Q4W |
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Reporting group description:

Participants who completed 9 cycles of the originally assigned treatment could switch to the open label extension. Participants enrolled received PRM-151 at a dose of 10mg/kg Q4W on days 1, 3, and 5 of first cycle of the open label phase and Day 1 of each subsequent 28 day cycle.

| | |
|-----------------------|------------------------------------------------------------|
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|-----------------------|------------------------------------------------------------|

Reporting group description:

Participants on a stable dose of ruxolitinib for at least 12 weeks, with no improvement in spleen during the last four weeks were assigned to receive PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles.

| | |
|-----------------------|------------------------------------------------------|
| Reporting group title | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib |
|-----------------------|------------------------------------------------------|

Reporting group description:

Participants who completed the main phase of treatment moved to the open label extension. They were treated with PRM-151 at a dose of 10 mg/kg administered as an IV infusion in combination with daily oral ruxolitinib on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle.

| | |
|-----------------------|---------------------------------------------------------------|
| Reporting group title | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) |
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Reporting group description:

Participants who received no treatment for MF in at least two weeks were assigned to treatment with single agent PRM-151 at a dose of 10 mg/kg administered as a 30 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for six cycles.

| | |
|-----------------------|----------------------------------------|
| Reporting group title | OLE Stage 1: RO7490677 10 mg/kg IV Q4W |
|-----------------------|----------------------------------------|

Reporting group description:

Participants who completed the main phase of treatment moved to the open label extension. They were treated with single agent PRM-151 at a dose of 10 mg/kg administered as an IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle.

| | |
|-----------------------|----------------------------------------------|
| Reporting group title | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W |
|-----------------------|----------------------------------------------|

Reporting group description:

Participants were treated with single agent PRM-151 at a dose of 3.0 mg/kg administered as a 60 minute IV infusion on Days 1, 3, and 5 of Cycle 1 and Day 1 of each subsequent 28 day cycle for nine cycles.

| Serious adverse events | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
|---------------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------|-----------------------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 11 / 33 (33.33%) | 14 / 32 (43.75%) |
| number of deaths (all causes) | 1 | 7 | 9 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Hepatic cancer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Myelofibrosis | | | |

| | | | |
|------------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Primary myelofibrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Transformation to acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Vascular disorders | | | |
| Dry gangrene | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Surgical and medical procedures | | | |
| Aortic valve replacement | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 2 / 32 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Organ failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Unevaluable event | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |

| | | | |
|----------------------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Infusion related reaction | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Osteoradionecrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Post procedural haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Acute myocardial infarction | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Hepatic encephalopathy | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 / 33 (0.00%) | 0 / 32 (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 |
| Bone marrow failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Extramedullary haemopoiesis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Pancytopenia | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral hernia, obstructive | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Melaena | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Oesophageal varices haemorrhage | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Portal hypertension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| Eczema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| 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 ulcer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder rupture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (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 |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Gastroenteritis | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 | 1 / 6 (16.67%) | 2 / 33 (6.06%) | 2 / 32 (6.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Pseudomonal sepsis | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 syncytial virus infection | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Wound infection | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (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 |

| Serious adverse events | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | OLE Stage 2: RO7490677 10 mg/kg IV Q4W | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|---------------------------------------------------------------------|--------------------------------------------------------------------|----------------------------------------------|---------------------------------------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 22 / 48 (45.83%) | 0 / 6 (0.00%) |
| number of deaths (all causes) | 2 | 7 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Hepatic cancer | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Malignant neoplasm progression | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Myelofibrosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| Primary myelofibrosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Transformation to acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 | | | |
| Dry gangrene | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Surgical and medical procedures | | | |

| | | | |
|---------------------------------------------------------|----------------|----------------|---------------|
| Aortic valve replacement subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Death | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Organ failure | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |

| | | | |
|----------------------------------------------------------------|---------------|----------------|---------------|
| Unevaluable event | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Investigations | | | |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 | | | |
| Fall | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Osteoradionecrosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Post procedural haematoma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone marrow failure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Extramedullary haemopoiesis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Leukocytosis | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Femoral hernia, obstructive | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Melaena | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Mouth haemorrhage | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Portal hypertension | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 | | | |
| Eczema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 ulcer | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Urinary bladder haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder rupture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|-------------------------------------------------|----------------|----------------|---------------|
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 viral | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (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 |
| Urosepsis | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (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 |

| Serious adverse events | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | OLE Stage 1: RO7490677 10 mg/kg IV Q4W |
|---------------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 1 / 7 (14.29%) | 5 / 13 (38.46%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Hepatic cancer | | | |

| | | | |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelofibrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Primary myelofibrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transformation to acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | | | |
| Dry gangrene | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Haematoma | | | |

| | | | |
|------------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Aortic valve replacement | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Death | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Organ failure | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |

| | | | |
|----------------------------------------------------------------|---------------|---------------|----------------|
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Unevaluable event | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | | | |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Hepatic enzyme increased | | | |

| | | | |
|-------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoradionecrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Post procedural haematoma | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |

| | | | |
|-------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Pericardial effusion | | | |

| | | | |
|-------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Bone marrow failure | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Extramedullary haemopoiesis | | | |

| | | | |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 / 5 (0.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral hernia, obstructive | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |

| | | | |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Cholelithiasis | | | |

| | | | |
|-------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Portal hypertension | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| 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 | | | |
| Eczema | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 ulcer | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 failure | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder rupture | | | |

| | | | |
|--------------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |

| | | | |
|-------------------------------------------------|----------------|---------------|----------------|
| Endocarditis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Infection | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia fungal | | | |

| | | | |
|-------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 viral | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 syncytial virus infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |

| | | | |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Wound infection | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (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 |

| | | | |
|---------------------------------------------------------------------|----------------------------------------------------|--|--|
| Serious adverse events | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 32 (43.75%) | | |
| number of deaths (all causes) | 6 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic cancer | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelofibrosis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Primary myelofibrosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transformation to acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Dry gangrene | | | |

| | | | |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Aortic valve replacement | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disease progression | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Inflammation | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|----------------------------------------------------------------|----------------|--|--|
| Organ failure | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Unevaluable event | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Eastern Cooperative Oncology Group performance status worsened | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoradionecrosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rib fracture | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery disease | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone marrow failure | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Extramedullary haemopoiesis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femoral hernia, obstructive | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal obstruction | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Melaena | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Varices oesophageal | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Portal hypertension | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Eczema | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary bladder haemorrhage | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary bladder rupture | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|-------------------------------------------------|----------------|--|--|--|
| Cellulitis | | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocarditis | | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis infectious | | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infection | | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral discitis | | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteomyelitis | | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Main Phase Stage 1: RO7490677 10 mg/kg IV QW + Ruxolitinib | Main Phase Stage 2: RO7490677 0.3 mg/kg IV Q4W | Main Phase Stage 2: RO7490677 10 mg/kg IV Q4W |
|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------|-----------------------------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 6 / 6 (100.00%) | 32 / 33 (96.97%) | 31 / 32 (96.88%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lipoma subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Neoplasm subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Squamous cell carcinoma subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 2 / 33 (6.06%) 2 | 0 / 32 (0.00%) 0 |
| Vascular disorders Haematoma subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Hot flush subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Hypertension subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 33 (3.03%) 1 | 1 / 32 (3.13%) 1 |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 33 (3.03%) 1 | 2 / 32 (6.25%) 2 |
| Chest discomfort subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Chest pain | | | |

| | | | |
|-----------------------------|----------------|-----------------|------------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Extravasation | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 8 / 33 (24.24%) | 11 / 32 (34.38%) |
| occurrences (all) | 3 | 9 | 12 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 2 | 1 |
| Ill-defined disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 6 / 33 (18.18%) | 9 / 32 (28.13%) |
| occurrences (all) | 0 | 8 | 10 |
| Pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 33 (6.06%) | 2 / 32 (6.25%) |
| occurrences (all) | 1 | 3 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 4 / 33 (12.12%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 4 | 3 |
| Swelling | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------------|---------------------|------------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Vessel puncture site bruise subjects affected / exposed occurrences (all) | 2 / 6 (33.33%) 5 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Social circumstances Blood product transfusion dependent subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 6 (33.33%) 2 | 10 / 33 (30.30%) 12 | 5 / 32 (15.63%) 5 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 4 / 33 (12.12%) 7 | 7 / 32 (21.88%) 8 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 33 (9.09%) 3 | 0 / 32 (0.00%) 0 |
| Epistaxis subjects affected / exposed occurrences (all) | 2 / 6 (33.33%) 3 | 5 / 33 (15.15%) 7 | 4 / 32 (12.50%) 11 |
| Hypoxia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Nasal dryness subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Oropharyngeal pain | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paranasal sinus discomfort | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Depression | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 33 (3.03%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|----------------------------------------|---------------|-----------------|----------------|
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 2 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 3 | 1 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 4 / 33 (12.12%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 8 | 2 |
| Weight decreased | | | |

| | | | |
|------------------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 6 / 33 (18.18%) | 8 / 32 (25.00%) |
| occurrences (all) | 0 | 7 | 11 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 1 | 3 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post-traumatic pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |

| | | | |
|--------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 1 | 3 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transfusion reaction | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 6 / 33 (18.18%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 9 | 1 |
| Headache | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 4 / 33 (12.12%) | 3 / 32 (9.38%) |
| occurrences (all) | 2 | 5 | 3 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 2 | 1 |
| Nerve compression | | | |

| | | | |
|--------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 3 | 1 |
| Sciatic nerve neuropathy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 5 / 33 (15.15%) | 3 / 32 (9.38%) |
| occurrences (all) | 1 | 11 | 6 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 2 | 3 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 5 / 33 (15.15%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 6 | 1 |
| Eye disorders | | | |
| Dry eye | | | |

| | | | |
|-----------------------------|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 3 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 5 / 33 (15.15%) | 4 / 32 (12.50%) |
| occurrences (all) | 0 | 7 | 5 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 2 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 4 / 33 (12.12%) | 4 / 32 (12.50%) |
| occurrences (all) | 0 | 5 | 6 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 8 / 33 (24.24%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 8 | 3 |

| | | | |
|---------------------------------|----------------|----------------|-----------------|
| Flatulence | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 33 (6.06%) | 5 / 32 (15.63%) |
| occurrences (all) | 1 | 2 | 5 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 33 (3.03%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 33 (3.03%) | 5 / 32 (15.63%) |
| occurrences (all) | 1 | 1 | 9 |
| Hepatobiliary disorders | | | |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatosplenomegaly | | | |

| | | | |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lichen planus | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 0 | 1 |
| Petechiae | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 0 | 3 |
| Rash | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Rash pruritic subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Skin induration subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Skin lesion subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 32 (3.13%) 1 |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 3 / 33 (9.09%) 3 | 2 / 32 (6.25%) 2 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 2 / 33 (6.06%) 2 | 0 / 32 (0.00%) 0 |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 33 (9.09%) 3 | 2 / 32 (6.25%) 2 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Groin pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint lock | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 2 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 3 | 2 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 33 (6.06%) | 1 / 32 (3.13%) |
| occurrences (all) | 2 | 3 | 1 |
| Infections and infestations | | | |
| Bronchitis | | | |

| | | | |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 5 | 1 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 2 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised infection | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lyme disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 1 | 3 |
| Oral herpes | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 4 | 3 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |

| | | | |
|-----------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 33 (6.06%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 33 (6.06%) | 1 / 32 (3.13%) |
| occurrences (all) | 2 | 4 | 1 |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 4 / 33 (12.12%) | 4 / 32 (12.50%) |
| occurrences (all) | 0 | 5 | 6 |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| Gout | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 1 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 33 (9.09%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 4 | 2 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 33 (3.03%) | 4 / 32 (12.50%) |
| occurrences (all) | 0 | 1 | 4 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 33 (3.03%) | 2 / 32 (6.25%) |
| occurrences (all) | 1 | 1 | 2 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron overload | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 33 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Main Phase Stage 1: RO7490677 10 mg/kg IV Every Week (QW) | OLE Stage 2: RO7490677 10 mg/kg IV Q4W | Main Phase Stage 1: RO7490677 10 mg/kg IV Q4W+ Ruxolitinib |
|------------------------------------------------------------------------|--------------------------------------------------------------------|----------------------------------------------|---------------------------------------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | 32 / 48 (66.67%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|------------------------------------------------------|----------------|----------------|----------------|
| Lipoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neoplasm | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Chills | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Early satiety | | | |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Extravasation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 5 / 48 (10.42%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 5 | 1 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ill-defined disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 48 (8.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 3 | 3 |
| Swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site bruise | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Social circumstances | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------|---------------------|-----------------------|---------------------|
| Blood product transfusion dependent subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 4 / 48 (8.33%) 4 | 1 / 6 (16.67%) 1 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 4 / 48 (8.33%) 4 | 0 / 6 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 2 / 6 (33.33%) 2 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 7 / 48 (14.58%) 16 | 1 / 6 (16.67%) 1 |
| Hypoxia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Nasal dryness subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 6 (0.00%) 0 |
| Paranasal sinus discomfort subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pleural effusion | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 48 (6.25%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Aspartate aminotransferase increased | | | |

| | | | |
|----------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 5 / 48 (10.42%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |

| | | | |
|--------------------------------------------------------------------------------------|--------------------|----------------------|---------------------|
| White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 3 / 48 (6.25%) 3 | 0 / 6 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Arthropod bite subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 5 / 48 (10.42%) 5 | 0 / 6 (0.00%) 0 |
| Eye contusion subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 3 / 48 (6.25%) 6 | 0 / 6 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Post-traumatic pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Road traffic accident subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 3 |
| Transfusion reaction | | | |

| | | | |
|--------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatic nerve neuropathy | | | |

| | | | |
|--------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 6 / 48 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 12 | 1 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 7 / 48 (14.58%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|----------------------------------|----------------|-----------------|----------------|
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 7 / 48 (14.58%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 7 | 2 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Gingival bleeding subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 6 (0.00%) 0 |
| Gingival pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 2 | 3 / 48 (6.25%) 5 | 0 / 6 (0.00%) 0 |
| Oral disorder subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 2 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Oral pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Retching subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Stomatitis subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 3 / 48 (6.25%) 4 | 0 / 6 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hepatobiliary disorders Hepatomegaly subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hepatosplenomegaly subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lichen planus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin induration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|-------------------------------------------------------------------------------------------------------------------|--------------------|---------------------|---------------------|
| Skin lesion subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 3 / 48 (6.25%) 3 | 1 / 6 (16.67%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 6 (0.00%) 0 |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Groin pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Joint lock subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| Joint swelling | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 48 (6.25%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 48 (8.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Diarrhoea infectious | | | |

| | | | |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lyme disease | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 48 (6.25%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |

| | | | |
|-----------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 5 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 48 (8.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 48 (4.17%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 48 (2.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron overload | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 48 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | OLE Stage 1: RO7490677 10 mg/kg IV Q4W + Ruxolitinib | Main Phase Stage 1: RO7490677 10 mg/kg IV Every 4 Weeks (Q4W) | OLE Stage 1: RO7490677 10 mg/kg IV Q4W |
|---------------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 5 (100.00%) | 6 / 7 (85.71%) | 12 / 13 (92.31%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Neoplasm | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Squamous cell carcinoma subjects affected / exposed occurrences (all) | 3 / 5 (60.00%) 3 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Vascular disorders | | | |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Hot flush subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Hypertension subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 7 (14.29%) 1 | 0 / 13 (0.00%) 0 |
| Chest discomfort subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Chest pain subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Chills subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 13 (7.69%) 2 |
| Early satiety subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Extravasation subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Fatigue | | | |

| | | | |
|------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 2 / 13 (15.38%) |
| occurrences (all) | 0 | 1 | 2 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ill-defined disorder | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 2 / 13 (15.38%) |
| occurrences (all) | 0 | 1 | 2 |
| Pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Swelling | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vessel puncture site bruise | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Social circumstances | | | |
| Blood product transfusion dependent | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders | | | |

| | | | |
|--------------------------------------------------------------------------------|---------------------|---------------------|----------------------|
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 3 / 5 (60.00%) 4 | 0 / 7 (0.00%) 0 | 2 / 13 (15.38%) 3 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 2 / 7 (28.57%) 2 | 0 / 13 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Hypoxia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Nasal dryness subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Paranasal sinus discomfort subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Pleural effusion subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Pneumothorax | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------------------|----------------|----------------|----------------|
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Contusion | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 3 | 0 | 1 |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Post-traumatic pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transfusion reaction | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound | | | |

| | | | |
|--------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 7 (0.00%) | 2 / 13 (15.38%) |
| occurrences (all) | 4 | 0 | 3 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 2 / 7 (28.57%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Sciatic nerve neuropathy | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |

| | | | |
|--------------------------------------------------|---------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 2 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 3 / 13 (23.08%) |
| occurrences (all) | 0 | 0 | 3 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal distension | | | |

| | | | |
|----------------------------------|----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 3 / 13 (23.08%) |
| occurrences (all) | 0 | 0 | 4 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival pain | | | |

| | | | |
|----------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 1 / 7 (14.29%) | 4 / 13 (30.77%) |
| occurrences (all) | 3 | 1 | 5 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 1 / 7 (14.29%) | 2 / 13 (15.38%) |
| occurrences (all) | 2 | 1 | 2 |
| Hepatobiliary disorders | | | |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatosplenomegaly | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lichen planus | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin induration | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |

| | | | |
|--------------------------------------------------|--------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Nocturia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 4 / 5 (80.00%) | 0 / 7 (0.00%) | 2 / 13 (15.38%) |
| occurrences (all) | 4 | 0 | 2 |
| Back pain | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint lock | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---------------------------------------|----------------|----------------|----------------|
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lyme disease | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 7 (14.29%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 3 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|-----------------------------------------|---------------|---------------|-----------------|
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 3 / 13 (23.08%) |
| occurrences (all) | 0 | 0 | 4 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 2 / 13 (15.38%) |
| occurrences (all) | 0 | 0 | 3 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Gout | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperuricaemia | | | |

| | | | |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Iron overload | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 7 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---------------------------------------------------------------------|----------------------------------------------------|--|--|
| Non-serious adverse events | Main Phase Stage 2: RO7490677 3 mg/kg IV Q4W | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 32 (93.75%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neoplasm | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders | | | |

| | | | |
|------------------------------------------------------|-----------------|--|--|
| Haematoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chills | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 5 | | |
| Early satiety | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Extravasation | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 32 (25.00%) | | |
| occurrences (all) | 10 | | |
| Gait disturbance | | | |

| | | | |
|-------------------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Ill-defined disorder | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 4 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 8 | | |
| Swelling | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vessel puncture site bruise | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Social circumstances | | | |
| Blood product transfusion dependent | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Cough | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 8 | | |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 8 / 32 (25.00%) | | |
| occurrences (all) | 10 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Epistaxis | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| Paranasal sinus discomfort | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|----------------------------------------------------------------------------------------------------------|----------------------|--|--|
| Sleep apnoea syndrome subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Upper-airway cough syndrome subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Psychiatric disorders Delirium subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 3 | | |
| Depression subjects affected / exposed occurrences (all) | 4 / 32 (12.50%) 4 | | |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 32 (3.13%) 1 | | |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 32 (12.50%) 7 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 5 / 32 (15.63%) 9 | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 4 | | |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Blood creatine phosphokinase increased | | | |

| | | | |
|------------------------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 4 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| Weight decreased | | | |
| subjects affected / exposed | 8 / 32 (25.00%) | | |
| occurrences (all) | 8 | | |
| Weight increased | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthropod bite | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Eye contusion | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Fall | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 7 | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Post-traumatic pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Transfusion reaction | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wound | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| Palpitations | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| Headache | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 8 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Sciatic nerve neuropathy | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | | |
| occurrences (all) | 8 | | |
| Increased tendency to bruise | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| Splenomegaly | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 5 | | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | | |
| occurrences (all) | 8 | | |
| Abdominal pain lower | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | | |
| occurrences (all) | 5 | | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Oral disorder | | | |

| | | | |
|----------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Retching | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| Hepatobiliary disorders | | | |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatosplenomegaly | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Ecchymosis | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperkeratosis | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lichen planus | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Night sweats | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 7 | | |
| Petechiae | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 6 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin induration | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-------------------------------------------------------------------------------------------------------------------|----------------------|--|--|
| Haematuria subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 5 / 32 (15.63%) 5 | | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 3 | | |
| Bone pain subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 3 | | |
| Groin pain subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Joint lock subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Joint swelling subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Muscle spasms subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 3 | | |
| Muscular weakness subjects affected / exposed occurrences (all) | 1 / 32 (3.13%) 2 | | |
| Musculoskeletal chest pain | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | | |
| occurrences (all) | 5 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---------------------------------------|----------------|--|--|
| Localised infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lyme disease | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Oral herpes | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences (all) | 1 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---------------------------------------------------------------------------------------------|----------------------|--|--|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | | |
| Urosepsis subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Metabolism and nutrition disorders | | | |
| Cachexia subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 4 / 32 (12.50%) 5 | | |
| Gout subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 5 | | |
| Hyperphosphataemia subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 4 / 32 (12.50%) 5 | | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | | |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Iron overload | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 22 February 2013 | The protocol was amended to clarify that participants could switch to different treatment arms after the completion of 6 cycles and that participants were evaluable for response after 4 weeks of treatment. The requirement for post infusion observation changed to four hours (from one hour) after all doses of PRM-151 through Cycle 2, Day 1 and for one hour after each subsequent dose. Specific instructions were provided for slowing or stopping PRM-151 infusion and for prophylaxis of infusion reactions (IR) for those who experienced IR(s). The IWG response criteria was assigned to the efficacy and some safety assessments. Gradation of treatment emergent non-hematological AEs considered applicable for the stopping rules to grade 3 was lowered. The timing of vital sign assessments were changed. Anti-drug antibody levels on Days 15 and 22 of Cycle 1 was included for participants receiving QW PRM-151, and on Day 15 for participants receiving Q4W dosing of PRM-151. The number of PK samples required was reduced. |
| 10 May 2013 | Added a summary of the acute infusion reactions seen in chronic toxicology studies and a summary of the root cause analysis and risk mitigation plan for humans; modified the PRM-151 infusion rate from 30 minutes to 60 minutes; clarified that participants in Cohort 2, receiving ruxolitinib should avoid strong CYP3A4 inhibitors; clarified that all acute infusion reactions should be managed according to guidelines; added Electrocardiogram (ECG) assessments at Day 1 of each cycle; clarified that if a participant experienced an acute infusion related reaction, a sample for anti-pentraxin-2 antibodies and a sample for cytokines would be collected; updated classification structure of AEs; increased safety surveillance measures; clarified that AEs would be followed beyond 30 days after the last dose if needed; clarified sample size calculations; clarified that no comparisons between treatment arms were to be performed; clarified that all participants that discontinued prior to completing 1 cycle of treatment were considered non responders; clarified that all participants that received at least 1 exposure to PRM-151 were included in the safety set; added the use of a Data Monitoring Committee (DMC). |
| 14 February 2014 | This protocol amendment clarified that stable disease with improvement in bone marrow fibrosis was called a bone marrow response. The requirements for continuing in the OLE portion of the study were included along with the dose calculated based on the participant's weight of Day 1 of each cycle. It explained that although serious adverse events (SAEs) were captured from time of informed consent, only for participants that received at least one dose of PRM-151; SAEs in screen failures were not captured. A post infusion ECG for Cycle 6 only for Day 1 (both weekly and every 4 weekly schedules) and Day 15 (weekly schedule only) was added. A clarification that Response Assessments were performed on Day 1 of each cycle and that the first post dose PK sample was at the end of the 60 minute infusion. Revised response criteria for myelofibrosis based on the IWG-MRT and European LeukemiaNet (ELN) consensus report was included into this amendment. |

| | |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 04 May 2015 | The protocol was amended to remove "Open Label" from the title of the study. The primary, secondary and exploratory objectives and endpoints were modified and additional exploratory objectives and endpoints were included. There were revisions to the study design. Modifications were made to the inclusion criteria as well as creating additional exclusion criteria. Efficacy assessments were modified by using the World Health Organization (WHO) bone marrow fibrosis grade, changes in hemoglobin, platelets, peripheral blood blasts, disease related symptoms, and spleen size. The role of the Data Monitoring Committee was clarified for Stage 2. The dosing amount for the study drug as well as the timing of the dose was modified and the use of ruxolitinib was clarified in this amendment. The method for assigning participants to treatment groups was clarified. Information regarding study blinding, and the procedure for breaking the blind was added. Removed the concomitant medication ruxolitinib and the requirement to record self administration of ruxolitinib. JAK kinase inhibitors were added to the list of excluded concomitant medications. The European Consensus on Grading of Bone Marrow Fibrosis to the WHO criteria for bone marrow fibrosis was revised. Testing for Cytokines and levels of mRNA and miRNA was removed and genetic testing of JAK2V617F, MPLW515, Calreticulin, ASXL1, EZH2, SRSF2, IDH1/2 was included. Information regarding the OLE portion of the study was included. The requirement to maintain a diary for all red blood cell (RBC) and platelet transfusions was added and the requirements for bone marrow biopsy and aspirate were updated. The reporting requirements and contact information for Adverse Events of Special Interest (AESIs) and reporting SAEs were updated. |
| 15 December 2016 | The protocol amendment added a loading dose for in participants in Stage 2 OLE portion of the study. Additional safety information from the IPF trial was included. Added clarification that DNA sampling was not mandatory for participants was added along with the note that the baseline blood sample for DNA sampling would also be used for the cytogenetic analysis. Removed cytogenetic analysis on marrow biopsy/aspirate. Modified the units of measurement of serum creatinine and clarified that spleen size would be measures by CT or MRI. Added clarification for contraception and adding highly effective methods to align with IB v10, which laboratories were considered central or local and information regarding pregnancy-testing requirements. Clarified that PRM-151 could be resumed when AE had resolved to Grade 1 or baseline. Added anti-pentraxin 2 antibodies collection for IRR and anti-pentraxin 2 antibodies and cytokines in the event of a suspected AE. Serious Treatment Emergent AEs (TEAEs) were removed from this version of the protocol. Clarification was added to allow for a wider visit window and to clarify window for visit, imaging procedures, laboratory assessments, transfusion diary and response assessments during Cycle 2 through 9, Day 1 as well as a wider visit window and to clarify the window allowed for visit, lab collection, transfusion diary recording at the end of study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported