



Clinical trial results: A Phase-Ib/II Study of Ruxolitinib and Pomalidomide Combination Therapy in Patients with Primary and Secondary Myelofibrosis Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-002431-29 |
| Trial protocol | DE |
| Global end of trial date | 27 April 2024 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 10 May 2025 |
| First version publication date | 10 May 2025 |
| Summary attachment (see zip file) | MPNSG_02-12_Final_report_BfArM_22Apr2025_final_version (MPNSG_02- 12_Final_report_BfArM_22Apr2025_final_version.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------------------|
| Sponsor protocol code | POMINC(MPNSG02-12) |
|-----------------------|--------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01644110 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University Hospital of Ulm |
| Sponsor organisation address | Albert-Einstein-Allee 23, Ulm, Germany, 89081 |
| Public contact | Clinical trials office IM III, University Hospital of Ulm, +49 73150045901, mpnsg.innere3@uniklinik-ulm.de |
| Scientific contact | Clinical trials office IM III, University Hospital of Ulm, +49 73150045901, mpnsg.innere3@uniklinik-ulm.de |

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 | 03 December 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 April 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 April 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the clinical efficacy of ruxolitinib and pomalidomide combination therapy in primary and secondary MF patients based on the consensus criteria of the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) (Tefferi A et al, 2006), extended by the criterion RBC-transfusion independence (RBC-TI) (Gale RP et al, 2011; Gale RP et al, 2012).

Protection of trial subjects:

Safety was assessed by evaluation the following: reported adverse events, clinical laboratory test results, vital signs measurements, ECG findings, chest X-ray, sonographic assessment of the spleen, physical examination findings, monitoring of concomitant medications. For each safety parameter, all findings whether normal or abnormal were recorded in the CRF.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 19 August 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 | Germany: 95 |
| Worldwide total number of subjects | 95 |
| EEA total number of subjects | 95 |

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) | 17 |
| From 65 to 84 years | 77 |

| | |
|-------------------|---|
| 85 years and over | 1 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

First patient in: 19 Aug 2013; Last patient in: 27 April 2021; last patient out: 27 April 2024; Interruption after 6 patients in April 2014 for safety analysis. Restart of recruitment in July 2014. 2nd interruption in February 2017 until approval of amended protocol version 2.0. Restart of recruitment in August 2017.

Pre-assignment

Screening details:

Diagnosis of myeloproliferative neoplasms (de novo or secondary (post PV or post ET)), anemia with hemoglobin < 10g/dl or transfusion-dependent anemia, splenomegaly > 11cm total diameter and/or leukoerythroblastosis, ECOG < 3

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 95 |
| Number of subjects completed | 92 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|-----------------------|
| Reason: Number of subjects | Protocol deviation: 3 |
|----------------------------|-----------------------|

Period 1

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

Arms

| | |
|------------------------------|----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 |

Arm description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. Pomalidomide could not be escalated or reduced (only discontinued in case of toxicities), but ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

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

Dosage and administration details:

1 capsule of 0,5 mg per day for 12 cycles

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

Dosage and administration details:

2 capsules of 5 mg twice daily at treatment start, escalation of 5 mg twice daily allowed after 4 weeks if platelet counts stable or increasing, maximum dosage 25 mg twice daily. For 12 cycles

| | |
|------------------|----------|
| Arm title | Cohort 2 |
|------------------|----------|

Arm description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. For Pomalidomide dose escalation is intended as follows: cycles 1-3 0,5 mg once daily; cycles 4-6 1 mg once daily; starting cycle 7 2 mg once daily (reduction/discontinuation allowed in case of toxicities). Ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

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

Dosage and administration details:

1 capsule of 0,5 mg (cycles 1-3), 1 mg (cycles 4-6) or 2 mg (start in cycle 7) per day for 12 cycles

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

Dosage and administration details:

2 capsules of 5 mg twice daily at treatment start, escalation of 5 mg twice daily allowed after 4 weeks if platelet counts stable or increasing, maximum dosage 25 mg twice daily. For 12 cycles

| Number of subjects in period 1^[1] | Cohort 1 | Cohort 2 |
|---|----------|----------|
| Started | 39 | 53 |
| Completed | 27 | 31 |
| Not completed | 12 | 22 |
| Adverse event, serious fatal | 3 | 3 |
| Consent withdrawn by subject | 3 | 6 |
| Adverse event, non-fatal | 1 | 6 |
| Progress of underlying disease | 3 | 1 |
| Transplantation | 1 | - |
| Lack of efficacy | 1 | 6 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 95 patients started with screening but only 92 were included into the treatment arms. 3 patients were screening failure due to protocol deviation.

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Cohort 1 |
|-----------------------|----------|

Reporting group description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. Pomalidomide could not be escalated or reduced (only discontinued in case of toxicities), but ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

| | |
|-----------------------|----------|
| Reporting group title | Cohort 2 |
|-----------------------|----------|

Reporting group description:

Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. For Pomalidomide dose escalation is intended as follows: cycles 1-3 0,5 mg once daily; cycles 4-6 1 mg once daily; starting cycle 7 2 mg once daily (reduction/discontinuation allowed in case of toxicities). Ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily.

| Reporting group values | Cohort 1 | Cohort 2 | Total |
|--|----------|----------|-------|
| Number of subjects | 39 | 53 | 92 |
| 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) | 7 | 10 | 17 |
| From 65-84 years | 32 | 42 | 74 |
| 85 years and over | 0 | 1 | 1 |
| Age continuous | | | |
| Units: years | | | |
| median | 72 | 70 | |
| full range (min-max) | 49 to 83 | 52 to 86 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 17 | 21 | 38 |
| Male | 22 | 32 | 54 |
| Type of myelofibrosis | | | |
| Units: Subjects | | | |
| Primary MF | 30 | 34 | 64 |
| Secondary MF | 9 | 18 | 27 |
| Unclassified MF | 0 | 1 | 1 |
| Bone marrow fibrosis grade | | | |
| Units: Subjects | | | |
| Grade 0 | 0 | 1 | 1 |
| Grade 1 | 5 | 4 | 9 |
| Grade 2 | 14 | 25 | 39 |

| | | | |
|--|----|----|----|
| Grade 3 | 15 | 20 | 35 |
| Missing | 5 | 3 | 8 |
| ECOG | | | |
| Units: Subjects | | | |
| ECOG 0 | 12 | 25 | 37 |
| ECOG 1 | 25 | 25 | 50 |
| ECOG 2 | 1 | 3 | 4 |
| Missing | 1 | 0 | 1 |
| Pretreated | | | |
| Pretreatment with any medications for myelofibrosis | | | |
| Units: Subjects | | | |
| yes | 22 | 33 | 55 |
| no | 17 | 20 | 37 |
| Pretreated with Ruxolitinib | | | |
| Units: Subjects | | | |
| yes | 6 | 23 | 29 |
| no | 33 | 30 | 63 |
| RBC transfusion dependent | | | |
| Units: Subjects | | | |
| yes | 10 | 19 | 29 |
| no | 29 | 34 | 63 |
| JAK2V617F Mutation | | | |
| Is a JAK2V617F Mutation available? | | | |
| Units: Subjects | | | |
| yes | 28 | 25 | 53 |
| no | 11 | 28 | 39 |
| MPL Mutation | | | |
| Is a MPM Mutation available? | | | |
| Units: Subjects | | | |
| yes | 3 | 8 | 11 |
| no | 36 | 45 | 81 |
| CALR Mutation | | | |
| Is a CALR Mutation available? | | | |
| Units: Subjects | | | |
| yes | 8 | 14 | 22 |
| no | 30 | 39 | 69 |
| Missing | 1 | 0 | 1 |
| Baseline DIPSS | | | |
| Units: Subjects | | | |
| Low | 1 | 0 | 1 |
| Intermediate - 1 | 6 | 5 | 11 |
| Intermediate - 2 | 27 | 39 | 66 |
| High | 5 | 9 | 14 |
| Any high risk mutation | | | |
| Is there any high risk mutation available (ASXL1, EZH2, SRSF2, IDH1+2, U2AF1, TP53)? | | | |
| Units: Subjects | | | |
| yes | 25 | 31 | 56 |
| no | 14 | 22 | 36 |
| ASXL1 Mutation | | | |
| Units: Subjects | | | |
| Yes | 16 | 22 | 38 |

| | | | |
|---|--------------|--------------|----|
| No | 23 | 31 | 54 |
| EZH2 Mutation Units: Subjects | | | |
| Yes | 4 | 7 | 11 |
| No | 35 | 46 | 81 |
| SRSF2 Mutation Units: Subjects | | | |
| Yes | 9 | 13 | 22 |
| No | 30 | 40 | 70 |
| IDH2 Mutation Units: Subjects | | | |
| Yes | 1 | 7 | 8 |
| No | 38 | 46 | 84 |
| U2AF1 Mutation Units: Subjects | | | |
| Yes | 5 | 7 | 12 |
| No | 34 | 46 | 80 |
| TP53 Mutation Units: Subjects | | | |
| Yes | 3 | 1 | 4 |
| No | 36 | 52 | 88 |
| Baseline spleen ultrasound Units: cm | | | |
| median | 17.9 | 17.0 | |
| full range (min-max) | 12.6 to 28.0 | 11.4 to 36.0 | - |
| Baseline spleen palpation Units: cm | | | |
| median | 5.0 | 3.0 | |
| full range (min-max) | 0 to 22.0 | 0 to 22.0 | - |
| Baseline hemoglobin value Units: g/dl | | | |
| median | 8.6 | 8.6 | |
| full range (min-max) | 5.4 to 11.7 | 5.9 to 10.8 | - |
| MPN SAF Baseline | | | |
| Mean values of selected questions of the Quality of Life Questionnaire MPN-SAF. | | | |
| Units: Points | | | |
| arithmetic mean | 2.98 | 2.62 | |
| standard deviation | ± 1.68 | ± 1.82 | - |
| Baseline thrombocytes value Units: Giga/l | | | |
| median | 249 | 247 | |
| full range (min-max) | 88 to 787 | 86 to 1240 | - |
| MIPSS | | | |
| Mutation-enhanced international prognostic score system | | | |
| Units: points | | | |
| median | 3 | 3 | |
| full range (min-max) | 1 to 3 | 1 to 3 | - |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Cohort 1 |
| Reporting group description: | |
| Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. Pomalidomide could not be escalated or reduced (only discontinued in case of toxicities), but ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily. | |
| Reporting group title | Cohort 2 |
| Reporting group description: | |
| Treatment started for all patients with a combination therapy of pomalidomide of 0,5 mg once daily and ruxolitinib 10 mg twice daily. For Pomalidomide dose escalation is intended as follows: cycles 1-3 0,5 mg once daily; cycles 4-6 1 mg once daily; starting cycle 7 2 mg once daily (reduction/discontinuation allowed in case of toxicities). Ruxolitinib was allowed to escalate after 4 weeks if platelet count was stable or increasing. Increase was allowed by 5 mg twice daily but the total dose of ruxolitinib may never exceed 25 mg twice daily. | |
| Subject analysis set title | Intention-to-treat |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Includes all patients who received the study medication at least once. | |

Primary: Response after 12 cycles

| | |
|---|--------------------------|
| End point title | Response after 12 cycles |
| End point description: | |
| Response was defined according to the IWG-MRT criteria (including complete remission, partial remission, clinical improvement), stable disease (Tefferi A et al, 2006), and red cell transfusion according to Gale et al 2010 and 2011, also progressive disease, relapse disease | |
| End point type | Primary |
| End point timeframe: | |
| The end point disease response was examined at the end of each cycle until at least cycle 12. | |

| End point values | Cohort 1 | Cohort 2 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 53 | | |
| Units: Subjects | | | | |
| Complete remission | 0 | 0 | | |
| Partial remission | 1 | 0 | | |
| Clinical improvement | 6 | 4 | | |
| Progressive disease | 1 | 0 | | |
| Relapse disease | 2 | 0 | | |
| Red blood cell transfusion dependent | 4 | 6 | | |
| Red blood cell transfusion independent | 1 | 2 | | |
| Clinical benefit | 0 | 16 | | |
| Missing | 13 | 23 | | |
| Stable disease | 11 | 2 | | |

Statistical analyses

| Statistical analysis title | Rate of response |
|--|-------------------------|
| Statistical analysis description: For cohort 1, response was defined as complete remission, partial remission, clinical improvement and red blood cell transfusion independency. For cohort 2, response was defined as complete remission, partial remission, clinical improvement and red blood cell transfusion independency, stable disease and clinical improvement. | |
| Comparison groups | Cohort 2 v Cohort 1 |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| Method | Binomialtest |
| Parameter estimate | Estimated response rate |
| Point estimate | 0.453 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| lower limit | 0.335 |

Notes:

[1] - For cohort 1, Simon's 2 stage design was used for analysis. The estimated response rate was 0.205 with one-sided 90% CI [0.123, 1].

According to amendment 2, additional 53 subjects was included as cohort 2 to decide whether the proportion responding, P, is less than or equal to 0.300 (null hypothesis) or greater than or equal to 0.500 (alternative). For cohort 2, a binomial test was used.

Secondary: Overall Survival

| | |
|--|------------------|
| End point title | Overall Survival |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Overall Survival: Number of patients and events by cohort with median survival time in months. | |

| End point values | Cohort 1 | Cohort 2 | | |
|----------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 53 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 38.4 (29.8 to 100) | 60.8 (29.8 to 999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

| | |
|-----------------|---------------------------|
| End point title | Progression free survival |
|-----------------|---------------------------|

End point description:

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

End point timeframe:

Progression free survival: Number of patients and events by cohort with median survival time in months

| End point values | Cohort 1 | Cohort 2 | | |
|----------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 53 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 29.8 (16.4 to 43) | 34.3 (21.2 to 999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration or response

| | |
|-----------------|----------------------|
| End point title | Duration or response |
|-----------------|----------------------|

End point description:

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

End point timeframe:

Duration of response from first response to loss of response (if occurred) or until end-of-FU (if no loss occurred)

| End point values | Cohort 1 | Cohort 2 | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 53 | | |
| Units: cycles | | | | |
| median (full range (min-max)) | 15 (8 to 126) | 9 (2 to 77) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from Informed Consent signature up to 28 days after last study drug administration or until all drug-related toxicities had been resolved, whichever was later.

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

Dictionary used

| | |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

| | |
|--------------------|-----|
| Dictionary version | 3.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Cohort 1 |
|-----------------------|----------|

Reporting group description:

All patients treated cohort 1

| | |
|-----------------------|----------|
| Reporting group title | Cohort 2 |
|-----------------------|----------|

Reporting group description:

All patients treated in cohort 2

| Serious adverse events | Cohort 1 | Cohort 2 | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 30 / 39 (76.92%) | 35 / 53 (66.04%) | |
| number of deaths (all causes) | 6 | 6 | |
| number of deaths resulting from adverse events | 6 | 6 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 6 / 39 (15.38%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | |
| Fibrosarcoma | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Malignant melanoma | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal adenocarcinoma alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Second primary malignancy alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vasculitis alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Breast operation | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint arthroplasty | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Knee arthroplasty | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Sudden cardiac death | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Chest pain | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Condition aggravated | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pain alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Reproductive system and breast disorders Acquired hydrocele alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders Dyspnoea alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary hypertension | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Delirium | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic haemorrhage | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute Myocardial infarction | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac valve disease | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiorenal syndrome | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Endocarditis fibroplastica | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachyarrhythmia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|----------------|----------------|--|
| Nervous system disorders | | | |
| Cerebral ischaemia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Dizziness | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraplegia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peripheral sensory neuropathy | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic haemorrhage | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenomegaly | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Spontaneous haematoma | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|--|
| <p>Ear and labyrinth disorders</p> <p>Deafness</p> <p>alternative dictionary used: MedDRA 27.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>1 / 39 (2.56%)</p> <p>0 / 1</p> <p>0 / 0</p> | <p>0 / 53 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | |
| <p>Gastrointestinal disorders</p> <p>Abdominal pain</p> <p>alternative dictionary used: MedDRA 27.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>2 / 39 (5.13%)</p> <p>0 / 2</p> <p>0 / 0</p> | <p>0 / 53 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | |
| <p>Ascites</p> <p>alternative dictionary used: MedDRA 27.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>1 / 39 (2.56%)</p> <p>0 / 1</p> <p>0 / 1</p> | <p>0 / 53 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | |
| <p>Diarrhoea</p> <p>alternative dictionary used: MedDRA 27.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 39 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | <p>1 / 53 (1.89%)</p> <p>0 / 1</p> <p>0 / 0</p> | |
| <p>Gastrointestinal haemorrhage</p> <p>alternative dictionary used: MedDRA 27.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 39 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | <p>2 / 53 (3.77%)</p> <p>0 / 2</p> <p>0 / 1</p> | |
| <p>Large intestine perforation</p> <p>alternative dictionary used: MedDRA 27.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 39 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | <p>1 / 53 (1.89%)</p> <p>0 / 1</p> <p>0 / 0</p> | |
| <p>Nausea</p> <p>alternative dictionary used: MedDRA 27.0</p> | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Soft tissue necrosis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis infective | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cystitis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile infection alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma infection alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | | |
|---|-----------------------------------|-----------------------------------|--|--|
| Nasopharyngitis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 39 (2.56%) 0 / 1 0 / 0 | 0 / 53 (0.00%) 0 / 0 0 / 0 | | |
| Oral viral infection alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 39 (0.00%) 0 / 0 0 / 0 | 1 / 53 (1.89%) 1 / 1 0 / 0 | | |
| Peritonitis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 39 (0.00%) 0 / 0 0 / 0 | 1 / 53 (1.89%) 0 / 1 0 / 0 | | |
| Pneumonia alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 5 / 39 (12.82%) 0 / 5 0 / 2 | 6 / 53 (11.32%) 4 / 7 1 / 1 | | |
| Sepsis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 39 (5.13%) 0 / 2 0 / 2 | 1 / 53 (1.89%) 1 / 1 0 / 0 | | |
| Septic shock alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 39 (2.56%) 0 / 1 0 / 1 | 0 / 53 (0.00%) 0 / 0 0 / 0 | | |
| Skin infection alternative dictionary used: MedDRA 27.0 | | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| alternative dictionary used: MedDRA 27.0 | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fluid retention | | | |
| alternative dictionary used: MedDRA 27.0 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Cohort 1 | Cohort 2 | |
|---|--|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 38 / 39 (97.44%) | 53 / 53 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Dermatology - Other (Basal cell carcinoma) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 3 | 1 | |
| Dermatology - Other (Spinaliom) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Secondary Malignancy (possibly related to cancer treatment) | Additional description: basal cell carcinoma | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sexual - Other (cyst right ovary) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Hematoma | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 5 / 53 (9.43%) | |
| occurrences (all) | 7 | 6 | |
| Hemorrhage - Other (defecation - black dyed) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hemorrhage - Other (eye) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hemorrhage - Other (Gums) | | | |

| | | |
|---|-----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Hemorrhage - Other (tongue) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Hemorrhage -Other (spitting of blood) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hemorrhage pulmonary - Nose | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 2 / 53 (3.77%) |
| occurrences (all) | 9 | 2 |
| Hemorrhage with surgery | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hemorrhage, GI - Oral cavity | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Hemorrhage, GU | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Thrombosis/embolism (vascular access) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Thrombosis/thrombus/embolism | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Vascular - Other (atherosklerotic artery on both sides) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Vascular - Other (circumference increase leg left) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Vasculitis | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vein injury - Extremity (lower) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Constitutional Symptoms - Other (exhaustion) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Constitutional Symptoms - Other (General disorder) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Constitutional Symptoms - Other (physical ability decreased) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Constitutional Symptoms - Other (reduced constitutional behavior) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Constitutional Symptoms - Other (reduced exercise capacity) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Constitutional Symptoms - Other (Reduced general condition) | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 0 / 53 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Constitutional Symptoms - Other (Vitamin D3 deficiency) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Constitutional Symptoms - Other (Weakness) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Fatigue | | | |

| | | | |
|--|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 16 / 39 (41.03%) 24 | 12 / 53 (22.64%) 13 | |
| Fever subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 5 | 8 / 53 (15.09%) 14 | |
| Insomnia subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 4 | 2 / 53 (3.77%) 2 | |
| Rigors/chills subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 3 | 1 / 53 (1.89%) 1 | |
| Sweating subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 4 | 3 / 53 (5.66%) 3 | |
| Weight gain subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 53 (3.77%) 2 | |
| Immune system disorders Allergic reaction subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 53 (0.00%) 0 | |
| Allergy - Other (vaccination reaction) subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Rhinitis subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 3 / 53 (5.66%) 3 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 8 | 8 / 53 (15.09%) 12 | |
| Dyspnea subjects affected / exposed occurrences (all) | 12 / 39 (30.77%) 19 | 21 / 53 (39.62%) 31 | |
| Hypoxia | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences (all) | 0 | 2 | |
| Nasal/paranasal reactions | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 2 | |
| Pain - Chest/thorax NOS | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Pain - Other (Chest wall) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain Pulmonary/Upper Respiratory: Chest/thorax NOS | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences (all) | 0 | 2 | |
| Pain Pulmonary/Upper Respiratory: Throat/pharynx/larynx | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 53 (1.89%) | |
| occurrences (all) | 3 | 1 | |
| Pulmonary - Other (breath sound) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pulmonary - Other (bronchitis) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pulmonary - Other (influenza) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pulmonary - Other (Pneumonia NOS) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |

| | | |
|---|----------------|----------------|
| Cardiac General - Other (Cardiac decompensation) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Valvular heart disease | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Edema: trunk/genital | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Intraop injury - Artery-aorta | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Left ventricular systolic dysfunction | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Supraventricular arrhythmia - Atrial fibrillation | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Cardiac General - Other (cardiac insufficiency) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cardiac General - Other (coronary artery disease) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cardiac General - Other (Edema pulmonary) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cardiac General - Other (Edema) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cardiac General - Other (heart insufficiency) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | | |
|--|----------------|----------------|--|
| Conduction abnormality - AV block second degree | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain Cardiavascular: Cardiac/heart | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Supraventricular arrhythmia - Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Cardiac Arrhythmia - Other (Arrhythmia) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac General - Other (cardiopulmonal congestion) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac General - Other (increased heart rate) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac General - Other (drop in blood pressure) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Conduction abnormality - AV Block-Third degree (Complete AV Block) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Edema: Head and neck | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Hypotension | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Edema: limb | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 4 / 53 (7.55%) | |
| occurrences (all) | 1 | 5 | |
| Hypertension | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 3 / 53 (5.66%) | |
| occurrences (all) | 4 | 3 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Apnea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences (all) | 0 | 2 | |
| Confusion | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Dizziness | | | |
| subjects affected / exposed | 11 / 39 (28.21%) | 10 / 53 (18.87%) | |
| occurrences (all) | 16 | 11 | |
| Mood alteration - Depression | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Mood alteration | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Neurology - Other (Concentration problem) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 2 | |
| Neurology - Other (Dysesthesia) | | | |

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|--|-----------------|------------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Neurology - Other (Panic attack) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Neurology - Other (Paresthesia) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Neurology - Other (Polyneuropathy) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Neurology - Other (speaking disorder) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Neurology - Other (Spinal disc herniation) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Neurology - Other (Tingling in feet) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Neuropathy - sensory | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 10 / 53 (18.87%) |
| occurrences (all) | 3 | 10 |
| Pain Neurology: Head/headache | | |
| subjects affected / exposed | 6 / 39 (15.38%) | 5 / 53 (9.43%) |
| occurrences (all) | 8 | 7 |
| Pain Neurology: Neuralgia/peripheral nerve | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Syncope (fainting) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Tremor | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 4 | |
| Blood and lymphatic system disorders | | | |
| Hemoglobin | | | |
| subjects affected / exposed | 17 / 39 (43.59%) | 23 / 53 (43.40%) | |
| occurrences (all) | 21 | 29 | |
| Platelets | | | |
| subjects affected / exposed | 6 / 39 (15.38%) | 8 / 53 (15.09%) | |
| occurrences (all) | 9 | 10 | |
| Blood - Other (leukocytosis) | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 53 (3.77%) | |
| occurrences (all) | 4 | 2 | |
| Blood - Other (Splenomegaly) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hemolysis | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Coagulation - Other (von Willebrandt syndrome type 2) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Iron overload | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 4 / 53 (7.55%) | |
| occurrences (all) | 1 | 4 | |
| Neutrophils | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 8 / 53 (15.09%) | |
| occurrences (all) | 1 | 8 | |
| Blood - Other (Thrombocytosis) | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 3 / 53 (5.66%) | |
| occurrences (all) | 4 | 3 | |
| Blood - Other (eosinophilia) | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Blood - Other (Blasts) | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 2 | |
| Blood - Other (Hematocrit decreased) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 3 | |
| Coagulation - Other (Coagulation disorder) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| INR | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Leukocytes | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 4 / 53 (7.55%) | |
| occurrences (all) | 0 | 4 | |
| Lymphatics - Other (Lymphnodes) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Blood - Other (red blood cells decreased) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences (all) | 0 | 2 | |
| Ear and labyrinth disorders | | | |
| Auditory/Ear - Other (Ear noises | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hearing (without monitoring program) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain Auditory/Ear: External ear | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Eye disorders | | | |

| | | | |
|-----------------------------------|----------------|----------------|--|
| Blurred vision | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 2 | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ocular - Other (Eye irritation) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ocular - Other (Herpes eye) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ocular - Other (Swollen eyes) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ocular - Other (Swollen tear sac) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ocular surface disease | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Watery eye | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Ascites | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 53 (1.89%) | |
| occurrences (all) | 3 | 1 | |
| Colitis | | | |

| | | |
|---|-----------------|------------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Constipation | | |
| subjects affected / exposed | 6 / 39 (15.38%) | 12 / 53 (22.64%) |
| occurrences (all) | 8 | 12 |
| Diarrhea | | |
| subjects affected / exposed | 9 / 39 (23.08%) | 15 / 53 (28.30%) |
| occurrences (all) | 11 | 21 |
| Distension | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Dry mouth | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Dysphagia | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Flatulence | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) |
| occurrences (all) | 0 | 3 |
| Gastritis | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 5 / 53 (9.43%) |
| occurrences (all) | 1 | 5 |
| Gastrointestinal - Other (loss of appetite) | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 53 (1.89%) |
| occurrences (all) | 2 | 1 |
| Gastrointestinal - Other (abdominal problems) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Gastrointestinal - Other (Condylomas) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 2 |
| Gastrointestinal - Other (Gastroenteritis) | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Gastrointestinal - Other (unspecific symptoms) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Heartburn | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 7 / 53 (13.21%) |
| occurrences (all) | 2 | 7 |
| Mucositis (clinical exam) - Pharynx | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Mucositis (clinical exam) - Oral cavity | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Nausea | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 5 / 53 (9.43%) |
| occurrences (all) | 5 | 6 |
| Pain Gastrointestinal: Abdomen NOS | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 3 / 53 (5.66%) |
| occurrences (all) | 13 | 9 |
| Pain Gastrointestinal: Dental/teeth/periodontal | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Pain Gastrointestinal: Oral cavity | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Pain Gastrointestinal: stomach | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 4 / 53 (7.55%) |
| occurrences (all) | 3 | 4 |
| Taste alteration | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Teeth | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 3 / 53 (5.66%) 4 | |
| Teeth development subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 53 (0.00%) 0 | |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 4 | 7 / 53 (13.21%) 9 | |
| Hepatobiliary disorders Hepatobiliary - Other (Steatosis) subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Pain Hepatobiliary/Pancreas: Liver subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 53 (3.77%) 2 | |
| Bruising subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 2 | 0 / 53 (0.00%) 0 | |
| Decubitus subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 53 (0.00%) 0 | |
| Dermatology - Other (perioral efflorescence) subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 53 (0.00%) 0 | |
| Dermatology - Other (diaper rash) subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Dermatology - Other (eczema) subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 53 (0.00%) 0 | |
| Dermatology - Other (Erysipel face) | | | |

| | | |
|---|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Dermatology - Other (excision of skin change) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dermatology - Other (furuncle right buttock) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Dermatology - Other (Herpes zoster) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Dermatology - Other (Skin changes) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) |
| occurrences (all) | 0 | 3 |
| Dermatology - Other (skin lesion) | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Dermatology - Other (swelling of lower leg) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dry skin | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) |
| occurrences (all) | 0 | 3 |
| Flushing | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Injection site reaction | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Pruritus | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 53 (3.77%) |
| occurrences (all) | 4 | 2 |
| Rash | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 53 (3.77%) | |
| occurrences (all) | 2 | 3 | |
| Ulceration | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Cystitis | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 3 / 53 (5.66%) | |
| occurrences (all) | 3 | 3 | |
| Pain - Renal/Genitourinary - Kidney | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Renal - Other (Chronic kidney disease) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Renal - Other (chronic renal insufficiency) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal - Other (fluid retention) | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 9 / 53 (16.98%) | |
| occurrences (all) | 9 | 10 | |
| Renal - Other (fluid retention/ edema) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal - Other (Prostata adenoma) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Renal - Other (recurrent dysuria) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal - Other (Renal stricture) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| renal - other (urinary obstruction) | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 0 / 53 (0.00%) 0 | |
| Renal failure subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 1 / 53 (1.89%) 1 | |
| Urinary frequency subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 2 | 3 / 53 (5.66%) 4 | |
| Urinary retention subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 1 / 53 (1.89%) 1 | |
| Endocrine disorders Endocrine - Other (partially hemorrhagic cyst) subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Endocrine - Other (Struma multinodosa) subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Hot flashes subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 3 / 53 (5.66%) 3 | |
| Musculoskeletal and connective tissue disorders Fracture subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 53 (3.77%) 2 | |
| Joint - function subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Muscle weakness subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 1 / 53 (1.89%) 1 | |
| Musculoskeletal - Other (arthrosis | | | |

| | | |
|---|------------------|------------------|
| left knee) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal - Other (bone pain, hip pain) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Musculoskeletal - Other (Bursitis) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Musculoskeletal - Other (Cervicobrachialgie) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal - Other (coxarthrosis) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal - Other (Cramps calves) | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Musculoskeletal - Other (Cramps) | | |
| subjects affected / exposed | 15 / 39 (38.46%) | 14 / 53 (26.42%) |
| occurrences (all) | 20 | 16 |
| Musculoskeletal - Other (disc herniation) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal - Other (hernia) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Musculoskeletal - Other (Lockjaw) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Musculoskeletal - Other (muscle tension neck) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | |
|--|-----------------|-----------------|
| Musculoskeletal - Other (muscle tensions) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal - Other (spasms) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal - Other (Swelling ankle) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) |
| occurrences (all) | 0 | 2 |
| Musculoskeletal - Other (Tendon rupture) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Musculoskeletal - Other (tension right shoulder) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pain - Other (Flank right) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Pain - Other (Groin) | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pain - Other (jaw) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pain - Other (left axilla) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Pain - Other (leg) | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pain Musculoskeletal: Back | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 8 / 53 (15.09%) |
| occurrences (all) | 7 | 8 |
| Pain Musculoskeletal: Bone | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 5 / 39 (12.82%) | 4 / 53 (7.55%) | |
| occurrences (all) | 11 | 4 | |
| Pain Musculoskeletal: Buttock | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Pain Musculoskeletal: Extremity- limb | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 1 / 53 (1.89%) | |
| occurrences (all) | 9 | 1 | |
| Pain Musculoskeletal: Joint | | | |
| subjects affected / exposed | 8 / 39 (20.51%) | 14 / 53 (26.42%) | |
| occurrences (all) | 8 | 16 | |
| Pain Musculoskeletal: Muscle | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 3 / 53 (5.66%) | |
| occurrences (all) | 10 | 3 | |
| Pain Musculoskeletal: Neck | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Infections and infestations | | | |
| Flu-like syndrome | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 1 / 53 (1.89%) | |
| occurrences (all) | 6 | 1 | |
| Infection - Other (Abscess) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 3 | |
| Infection - Other (aspiration pneumonia) | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Infection - Other (common cold) | | | |
| subjects affected / exposed | 8 / 39 (20.51%) | 6 / 53 (11.32%) | |
| occurrences (all) | 11 | 10 | |
| Infection - Other (COVID 19 Infection) | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 53 (3.77%) | |
| occurrences (all) | 2 | 2 | |
| Infection - Other (erysipiel) | | | |

| | | |
|---|-----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection - Other (Follikulitis) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection - Other (foot) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection - Other (General, Blood) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection - Other (Herpes zoster) | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 2 / 53 (3.77%) |
| occurrences (all) | 5 | 3 |
| Infection - Other (Left digitus medius) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection - Other (phlegmon) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection - Other (Pneumonia) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection - Other (Sepsis) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection - Other (Skin) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection - Other (sore throat) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Infection - Other (Urosepsis) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |

| | | |
|--|----------------|----------------|
| Infection - Other (wound) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection with grade 3 or 4 neutrophils- Liver | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection with grade 3 or 4 neutrophils- pharynx | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection with grade 3 or 4 neutrophils | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection with grade 3 or 4 neutrophils- Urinary tract NOS | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection with normal ANC | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection with normal ANC - Upper airway NOS | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection with unknown ANC - Bronchus | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Infection with unknown ANC - pharynx | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection with unknown ANC - Upper airway NOS | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection with unknown ANC - Urinary tract NOS | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infection Dermatology/Skin: Lip/perioral | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 53 (3.77%) |
| occurrences (all) | 2 | 2 |
| Infection Gastrointestinal: Abdomen NOS | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 6 / 53 (11.32%) |
| occurrences (all) | 6 | 6 |
| Infection Gastrointestinal: Dental- tooth | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Infection Gastrointestinal: Oral cavity-gums (gingivitis) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection Musculoskeletal: Joint | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) |
| occurrences (all) | 1 | 1 |
| Infection Ocular: Conjunctiva | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 53 (1.89%) |
| occurrences (all) | 2 | 1 |
| Infection Ocular: Eye NOS | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Infection Pulmonary/Upper Respiratory: Bronchus | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 3 / 53 (5.66%) |
| occurrences (all) | 8 | 3 |
| Infection Pulmonary/Upper Respiratory: Lung (pneumonia) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 53 (5.66%) |
| occurrences (all) | 0 | 3 |
| Infection Pulmonary/Upper Respiratory: Pharynx | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |

| | | | |
|---|-----------------|------------------|--|
| Infection Pulmonary/Upper Respiratory: Sinus | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Infection Pulmonary/Upper Respiratory: Upper aerodigestive NOS | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infection Pulmonary/Upper Respiratory: Upper airway NOS | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 13 / 53 (24.53%) | |
| occurrences (all) | 6 | 14 | |
| Infection Renal/Genitourinary: Bladder (urinary) | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Infection Renal/Genitourinary: Prostate | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Infection Renal/Genitourinary: Urinary tract NOS | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 8 / 53 (15.09%) | |
| occurrences (all) | 6 | 9 | |
| Infection Sexual/Reproductive Function: Pelvis NOS | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| ALT | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 1 / 53 (1.89%) | |
| occurrences (all) | 5 | 1 | |
| AST | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 53 (1.89%) | |
| occurrences (all) | 2 | 1 | |
| Cholesterol | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Creatinine | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 9 / 39 (23.08%) | 2 / 53 (3.77%) |
| occurrences (all) | 9 | 3 |
| GGT | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Hyperkalemia | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 53 (1.89%) |
| occurrences (all) | 2 | 1 |
| Hyperuricemia | | |
| subjects affected / exposed | 8 / 39 (20.51%) | 6 / 53 (11.32%) |
| occurrences (all) | 9 | 6 |
| Hypoalbuminemia | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 53 (1.89%) |
| occurrences (all) | 0 | 1 |
| Hypocalcemia | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 53 (0.00%) |
| occurrences (all) | 2 | 0 |
| Hypokalemia | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 53 (3.77%) |
| occurrences (all) | 2 | 2 |
| Metabolic/Lab - Other (Hyperphosphatemia) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 53 (0.00%) |
| occurrences (all) | 1 | 0 |
| Metabolic/Lab - Other (Iron deficiency) | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) |
| occurrences (all) | 0 | 2 |
| Metabolic/Lab - Other (LDH increase) | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 3 / 53 (5.66%) |
| occurrences (all) | 1 | 3 |
| Metabolic/Lab - Other (Urea high) | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 53 (0.00%) |
| occurrences (all) | 4 | 0 |
| Metabolic/Lab - Other (Vitamin D deficiency) | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 53 (3.77%) | |
| occurrences (all) | 0 | 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 16 December 2013 | Urgent Amendment: Ruxolitinib was initially dispensed in bottles. This urgent amendment was necessary as Ruxolitinib was not available in bottles anymore but only in blisters. The urgent amendment was implemented in protocol version 1.4 |
| 16 April 2014 | Amendment 1.4 (07.01.2024): Exclusion Criteria added "Patient treatment with Ruxolitinib within a 14 days time period before Screening phase"; Implementation of tuberculosis tests; bone marrow biopsy and aspiration obtained at baseline, end of cycle 6, end of cycle 12 (biopsy: reference lab Hannover and Freiburg, aspiration: reference lab Ulm); Ruxolitinib dispensed in blisters (see also urgent amendment); parameter haptoglobin added. |
| 06 June 2017 | Amendment V 2.0 (28.03.2017): cohort 2 implemented: Pomalidomid 0,5 mg for 3 cycles, afterwards 1 mg for 3 cycles, starting cycle 7 2 mg; no change for Ruxolitinib; sample size increased: cohort 2 intended patient sample size n=53; study end changed to May 2022; explorative response criteria clinical benefit added; pregnancy prevention plan updated; Pomalidomid will be dispensed in wallets, not in bottles anymore. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---------------|--|--------------|
| 25 March 2014 | The POMINC study was interrupted for a safety analysis after enrollment of 6 patients and an observation period of each patient of at least one cycles (28 days) on 25-Mar-2014. This was outlined in the protocol (12.3.4). As the LKP, the trial coordinator, the statistician and the DSMB didn't have any safety concerns the study restarted recruitment on 02-Jul-2014 | 02 July 2014 |

Notes:

Limitations and caveats

None reported