



Clinical trial results:

A Randomized, Double-Blind Phase 2 Study of Ruxolitinib or Placebo in Combination With Pemetrexed/Cisplatin and Pemetrexed Maintenance for Initial Treatment of Subjects With Nonsquamous Non-Small Cell Lung Cancer That Is Stage IIIB, Stage IV, or Recurrent

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-001436-10 |
| Trial protocol | IT DK ES NL PT |
| Global end of trial date | 21 June 2016 |

Results information

| | |
|--------------------------------|--|
| Result version number | v3 (current) |
| This version publication date | 09 November 2017 |
| First version publication date | 10 August 2017 |
| Version creation reason | <ul style="list-style-type: none">• New data added to full data set• Correction of full data set Additional information received for safety data to be added. |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | INCB 18424-266 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02119650 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Incyte Corporation |
| Sponsor organisation address | 1801 Augustine Cut-Off, Wilmington, DE, United States, 19803 |
| Public contact | Incyte Corporation, Incyte Corporation Call Centre, +44 (0)330 100 3677, globalmedinfo@incyte.com |
| Scientific contact | Incyte Corporation, Incyte Corporation Call Centre, +44 (0)330 100 3677, globalmedinfo@incyte.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 21 June 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 June 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 June 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

- Part 1: To evaluate the safety and tolerability of ruxolitinib in combination with pemetrexed/cisplatin and select a dose for further evaluation
 - Part 2: To evaluate and compare the OS of subjects with nonsquamous NSCLC that is Stage IIIB, Stage IV, or recurrent when treated with ruxolitinib or placebo in combination with pemetrexed/cisplatin and subsequently pemetrexed maintenance
-

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Guidelines.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 February 2014 |
| 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 | Netherlands: 2 |
| Country: Number of subjects enrolled | Portugal: 4 |
| Country: Number of subjects enrolled | Spain: 17 |
| Country: Number of subjects enrolled | Denmark: 6 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | United States: 31 |
| Worldwide total number of subjects | 76 |
| EEA total number of subjects | 45 |

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) | 49 |
| From 65 to 84 years | 27 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 42 study centers (25 in the United States, 4 in Spain, 3 in France, 3 in Portugal, 2 in Denmark, 2 in Germany, 2 in Italy, 1 in the Netherlands).

Pre-assignment

Screening details:

Randomized, Double-Blind Portion:

Anticipated duration of treatment for an individual subject was approximately 8 months: up to 28 days for screening and baseline.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin |

Arm description:

Ruxolitinib was self-administered as a 15 mg twice daily (BID) oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

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

Dosage and administration details:

5 mg tablets to be administered by mouth at dose selected from safety run-in phase (Ruxolitinib 15 mg twice daily (BID)).

| | |
|--|-----------------|
| Investigational medicinal product name | Pemetrexed |
| Investigational medicinal product code | |
| Other name | Alimta® |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

500 mg/m² administered as an intravenous infusion over 10 minutes on Day 1 of each 21-day cycle.

| | |
|--|-----------------|
| Investigational medicinal product name | Cisplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

75 mg/m² infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion.

| | |
|------------------|---|
| Arm title | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin |
|------------------|---|

Arm description:

Matching placebo was self-administered as a 15 mg BID oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg matching placebo tablets to be administered by mouth.

| | |
|--|-----------------|
| Investigational medicinal product name | Pemetrexed |
| Investigational medicinal product code | |
| Other name | Alimta® |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

500 mg/m² administered as an intravenous infusion over 10 minutes on Day 1 of each 21-day cycle.

| | |
|--|-----------------|
| Investigational medicinal product name | Cisplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

75 mg/m² infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion.

| Number of subjects in period 1 | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin |
|---------------------------------------|---|---|
| Started | 39 | 37 |
| Completed | 14 | 11 |
| Not completed | 25 | 26 |
| Multiple reasons for termination | 2 | 1 |
| Physician decision | - | 2 |
| Disease progression | 11 | 14 |
| Adverse event, non-fatal | 3 | 4 |
| Subject decision | 2 | 3 |
| Death | 5 | 1 |
| Noncompliance with study treatment | 1 | 1 |
| Study terminated by the sponsor | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin |
|-----------------------|---|

Reporting group description:

Ruxolitinib was self-administered as a 15 mg twice daily (BID) oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

| | |
|-----------------------|---|
| Reporting group title | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin |
|-----------------------|---|

Reporting group description:

Matching placebo was self-administered as a 15 mg BID oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

| Reporting group values | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin n | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin n | Total |
|---|--|--|-------|
| Number of subjects | 39 | 37 | 76 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 26 | 23 | 49 |
| From 65-84 years | 13 | 14 | 27 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 61.6 | 62 | |
| standard deviation | ± 8.85 | ± 8.55 | - |
| Gender categorical Units: Subjects | | | |
| Female | 15 | 14 | 29 |
| Male | 24 | 23 | 47 |
| Body Mass Index (BMI) Units: kg/m ² | | | |
| arithmetic mean | 27.67 | 27.65 | |
| standard deviation | ± 6.402 | ± 7.26 | - |

End points

End points reporting groups

| | |
|-----------------------|---|
| Reporting group title | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin |
|-----------------------|---|

Reporting group description:

Ruxolitinib was self-administered as a 15 mg twice daily (BID) oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

| | |
|-----------------------|---|
| Reporting group title | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin |
|-----------------------|---|

Reporting group description:

Matching placebo was self-administered as a 15 mg BID oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

Primary: Overall Survival (OS)

| | |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

Overall survival is defined as the time from randomization to death due to any cause. Participants without death observed at the time of the analysis were censored at last date known to be alive. The median overall survival time was estimated using the Kaplan-Meier method. Overall survival was compared between treatment groups using log-rank test.

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

End point timeframe:

Randomization until death due to any cause; up to 16 months or data cutoff 11FEB2016.

| End point values | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 ^[1] | 37 ^[2] | | |
| Units: months | | | | |
| median (confidence interval 80%) | 7.5 (5.7 to 999.99) | 5.9 (4 to 999.99) | | |

Notes:

[1] - (ITT) population.

999.99= Not evaluable due to insufficient number of participants with events.

[2] - (ITT) population.

999.99= Not evaluable due to insufficient number of participants with events.

Statistical analyses

| | |
|----------------------------|------------------|
| Statistical analysis title | Overall Survival |
|----------------------------|------------------|

| | |
|-------------------|---|
| Comparison groups | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin |
|-------------------|---|

| | |
|---|---|
| | v Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin |
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7562 ^[3] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.877 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.509 |
| upper limit | 1.51 |

Notes:

[3] - The 2-sided p-value was calculated based on the log-rank test and stratified by modified Glasgow Prognostic Score (mGPS).

Secondary: Progression-free Survival (PFS)

| | |
|-----------------|---------------------------------|
| End point title | Progression-free Survival (PFS) |
|-----------------|---------------------------------|

End point description:

PFS is defined as the time from randomization until the earliest date of disease progression determined by investigator assessment of objective radiographic disease assessments per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, or death due to any cause if sooner. Progressive Disease (PD) is defined using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as at least a 20% increase in the sum of the Longest Diameter (LD) of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions, unequivocal progression of non-target lesions or increase in disease burden for subjects with only nonmeasurable disease.

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

End point timeframe:

Randomization to disease progression, or death due to any cause if sooner; up to 16 months or to the data cutoff 11FEB2016.

| End point values | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 ^[4] | 37 ^[5] | | |
| Units: months | | | | |
| number (not applicable) | 0 | 0 | | |

Notes:

[4] - PFS was not conducted due to early termination and insufficient number of participants with events.

[5] - PFS was not conducted due to early termination and insufficient number of participants with events.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

| | |
|-----------------|-------------------------------|
| End point title | Objective Response Rate (ORR) |
|-----------------|-------------------------------|

End point description:

Objective response rate determined by radiographic disease assessments per RECIST (v1.1), by investigator assessment and was defined as the percentage of participants with Complete Response (CR) or Partial Response (PR) by Response Evaluation Criteria in Solid Tumours (RECIST) at any post baseline visit. Per Response Evaluation Criteria In Solid Tumours Criteria (RECIST) for target lesions and assessed by computed tomography (CT) and/or magnetic resonance imaging (MRI) : Complete Response (CR), Disappearance of all target and non-target lesions; Partial Response (PR), $\geq 30\%$ decrease in the sum of the longest diameter of target lesions with no worsening of non-target lesions and no new lesions; Overall Response (OR) = CR + PR.

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

End point timeframe:

Baseline through end of study; up to 16 months or to the data cutoff 11FEB2016.

| End point values | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Cisplatin | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 ^[6] | 37 ^[7] | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Overall Response | 12 | 13 | | |
| Complete Response | 0 | 0 | | |
| Partial Response | 12 | 13 | | |
| Stable Disease | 4 | 5 | | |
| Progressive Disease | 6 | 4 | | |
| Unable to Evaluate | 2 | 3 | | |
| Not Assessed | 15 | 12 | | |

Notes:

[6] - The intent-to-treat (ITT) population consisted of participants that were randomized in the study.

[7] - The intent-to-treat (ITT) population consisted of participants that were randomized in the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

For objective responders, the duration of response is defined as the difference of the end of response and the start of response. The start of a response was the first visit where the subject achieves PR or better based on RECIST v1.1 criteria. The end of response was the first visit after PD based on RECIST v1.1 criteria.

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

End point timeframe:

From the start of response to the end of response; up to 16 months or to the data cutoff 11FEB2016.

| End point values | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Ci splat | Double-Blind Treatment: Placebo Plus Pemetrexed/Ci splat | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 ^[8] | 13 ^[9] | | |
| Units: weeks | | | | |
| median (confidence interval 80%) | 20.14 (18 to 30.71) | 12.14 (6 to 24) | | |

Notes:

[8] - The intent-to-treat (ITT) population consisted of participants that were randomized in the study.

[9] - The intent-to-treat (ITT) population consisted of participants that were randomized in the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With Treatment-emergent Adverse Events (TEAEs)

| | |
|-----------------|---|
| End point title | Participants With Treatment-emergent Adverse Events (TEAEs) |
|-----------------|---|

End point description:

A treatment-emergent AE was defined as an event occurring after exposure to at least 1 dose of study drug (ruxolitinib or placebo). A treatment-related AE was defined as an event with a definite, probable, or possible causality to study medication. A serious AE is an event resulting in death, hospitalization, persistent or significant disability/incapacity, or is life threatening, a congenital anomaly/birth defect or requires medical or surgical intervention to prevent 1 of the outcomes above. The intensity of an AE was graded according to the National Cancer Institute common terminology criteria for adverse events (NCI-CTCAE) version 4.03: Grade 1 (Mild); Grade 2 (Moderate); Grade 3 (Severe); Grade 4 (life-threatening).

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

End point timeframe:

Baseline through approximately 30 days post treatment discontinuation; up to 16 months or to the data cutoff 11FEB2016.

| End point values | Double-Blind Treatment: Ruxolitinib plus Pemetrexed/Ci splat | Double-Blind Treatment: Placebo Plus Pemetrexed/Ci splat | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 ^[10] | 37 ^[11] | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Participants who had any TEAEs | 39 | 36 | | |
| Participants who had treatment-related TEAEs | 16 | 28 | | |
| Participants with any serious TEAE | 19 | 16 | | |

| | | | | |
|--|----|----|--|--|
| Participants who had Grade 3 or higher TEAEs | 25 | 22 | | |
| Participants with a fatal TEAE | 4 | 4 | | |
| TEAEs related to reference therapy | 30 | 35 | | |
| Participants who were hospitalized due to TEAEs | 16 | 15 | | |
| Participants who discontinued drug due to TEAEs | 2 | 4 | | |
| Participants who interrupted drug due to TEAEs | 11 | 15 | | |
| Discontinued reference therapy due to TEAEs | 4 | 7 | | |
| Interrupted reference therapy due to TEAEs | 8 | 7 | | |
| Participants given concomitant meds due to TEAEs | 36 | 32 | | |
| Procedure/nondrug therapy due to TEAEs | 17 | 12 | | |

Notes:

[10] - Safety evaluable population consisted of all participants exposed to at least 1 dose of study drug.

[11] - Safety evaluable population consisted of all participants exposed to at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study medication through approximately 30 days post treatment discontinuation; up to 16 months or to the data cutoff 11FEB2016.

Adverse event reporting additional description:

The safety evaluable population consisted of all participants exposed to at least 1 dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Double-Blind Treatment: Ruxolitinib + Pemetrexed/Cisplatin |
|-----------------------|--|

Reporting group description:

Ruxolitinib was self-administered as a 15 mg BID oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

| | |
|-----------------------|---|
| Reporting group title | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin |
|-----------------------|---|

Reporting group description:

Matching placebo was self-administered as a 15 mg BID oral treatment during the randomized, double-blind treatment, without regard to food. Pemetrexed 500 mg/m² was administered as an intravenous infusion over 10 minutes, and 75 mg/m² Cisplatin was infused over 2 hours beginning 30 ± 5 minutes after the end of the pemetrexed infusion on Day 1 of each 21-day cycle (Treatment Cycles).

| Serious adverse events | Double-Blind Treatment: Ruxolitinib + Pemetrexed/Cisplatin | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 39 (48.72%) | 16 / 37 (43.24%) | |
| number of deaths (all causes) | 4 | 4 | |
| number of deaths resulting from adverse events | 4 | 4 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastatic pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 37 (5.41%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary toxicity | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Confusional state | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Chemical peritonitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VIth nerve disorder | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (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 | | | |
| Anemia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Diplopia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholangitis acute | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Pain in extremity subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia subjects affected / exposed | 3 / 39 (7.69%) | 3 / 37 (8.11%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis subjects affected / exposed | 1 / 39 (2.56%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Septic shock subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural infection subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection subjects affected / exposed | 1 / 39 (2.56%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection staphylococcal subjects affected / exposed | 0 / 39 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 37 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

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

| Non-serious adverse events | Double-Blind Treatment: Ruxolitinib + Pemetrexed/Cisplatin | Double-Blind Treatment: Placebo Plus Pemetrexed/Cisplatin | |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 37 / 39 (94.87%) | 36 / 37 (97.30%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 37 (5.41%) | |
| occurrences (all) | 3 | 3 | |
| Fatigue | | | |
| subjects affected / exposed | 13 / 39 (33.33%) | 14 / 37 (37.84%) | |
| occurrences (all) | 15 | 14 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 8 / 39 (20.51%) | 5 / 37 (13.51%) | |
| occurrences (all) | 8 | 5 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 4 / 37 (10.81%) | |
| occurrences (all) | 7 | 5 | |
| Asthenia | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 12 / 37 (32.43%) | |
| occurrences (all) | 9 | 17 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences (all) | 0 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------------|-----------------------|--|
| Acute respiratory failure subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 37 (5.41%) 2 | |
| Cough subjects affected / exposed occurrences (all) | 6 / 39 (15.38%) 6 | 9 / 37 (24.32%) 11 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 8 | 9 / 37 (24.32%) 16 | |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 1 / 37 (2.70%) 1 | |
| Nasal congestion subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 37 (5.41%) 2 | |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 37 (5.41%) 2 | |
| Haemoptysis subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 3 / 37 (8.11%) 3 | |
| Productive cough subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 37 (5.41%) 2 | |
| Wheezing subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 37 (5.41%) 2 | |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 37 (5.41%) 2 | |
| Depression subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 2 / 37 (5.41%) 2 | |
| Insomnia | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 3 / 37 (8.11%) 3 | |
| Investigations | | | |
| Blood calcium decreased subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 37 (5.41%) 2 | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 5 | 2 / 37 (5.41%) 2 | |
| Weight decreased subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 4 | 3 / 37 (8.11%) 3 | |
| C-reactive protein increased subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 3 / 37 (8.11%) 3 | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 3 / 37 (8.11%) 3 | |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 37 (5.41%) 2 | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 6 / 37 (16.22%) 7 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 3 | 6 / 37 (16.22%) 6 | |
| Headache subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 5 | 2 / 37 (5.41%) 2 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 4 | 0 / 37 (0.00%) 0 | |
| Peripheral sensory neuropathy | | | |

| | | | |
|--|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 3 | 3 / 37 (8.11%) 4 | |
| Syncope subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 2 / 37 (5.41%) 4 | |
| Blood and lymphatic system disorders | | | |
| Anemia subjects affected / exposed occurrences (all) | 15 / 39 (38.46%) 23 | 12 / 37 (32.43%) 15 | |
| Neutropenia subjects affected / exposed occurrences (all) | 8 / 39 (20.51%) 15 | 4 / 37 (10.81%) 6 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 5 | 0 / 37 (0.00%) 0 | |
| Ear and labyrinth disorders | | | |
| Tinnitus subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 4 / 37 (10.81%) 4 | |
| Ototoxicity subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 4 / 37 (10.81%) 5 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 2 / 37 (5.41%) 2 | |
| Constipation subjects affected / exposed occurrences (all) | 13 / 39 (33.33%) 14 | 13 / 37 (35.14%) 15 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 9 / 39 (23.08%) 9 | 10 / 37 (27.03%) 12 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 4 / 37 (10.81%) 5 | |
| Dysphagia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 37 (5.41%) | |
| occurrences (all) | 2 | 2 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 20 / 39 (51.28%) | 32 / 37 (86.49%) | |
| occurrences (all) | 25 | 48 | |
| Stomatitis | | | |
| subjects affected / exposed | 10 / 39 (25.64%) | 7 / 37 (18.92%) | |
| occurrences (all) | 12 | 11 | |
| Vomiting | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | 12 / 37 (32.43%) | |
| occurrences (all) | 11 | 18 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 37 (2.70%) | |
| occurrences (all) | 2 | 1 | |
| Rash | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 4 / 37 (10.81%) | |
| occurrences (all) | 1 | 4 | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 37 (2.70%) | |
| occurrences (all) | 2 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 37 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Back pain | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 4 / 37 (10.81%) | |
| occurrences (all) | 5 | 4 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences (all) | 0 | 3 | |
| Musculoskeletal chest pain | | | |

| | | | |
|------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 37 (2.70%) | |
| occurrences (all) | 2 | 2 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 37 (2.70%) | |
| occurrences (all) | 2 | 1 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 37 (8.11%) | |
| occurrences (all) | 0 | 3 | |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 0 / 37 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Infections and infestations | | | |
| Candida infection | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 37 (5.41%) | |
| occurrences (all) | 1 | 2 | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 37 (5.41%) | |
| occurrences (all) | 1 | 2 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 37 (2.70%) | |
| occurrences (all) | 3 | 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) | |
| occurrences (all) | 0 | 2 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 3 / 37 (8.11%) | |
| occurrences (all) | 1 | 3 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | |
|-----------------------------|-----------------|------------------|
| subjects affected / exposed | 5 / 39 (12.82%) | 14 / 37 (37.84%) |
| occurrences (all) | 7 | 14 |
| Dehydration | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 2 / 37 (5.41%) |
| occurrences (all) | 5 | 2 |
| Hypokalaemia | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 7 / 37 (18.92%) |
| occurrences (all) | 3 | 7 |
| Hyponatraemia | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 3 / 37 (8.11%) |
| occurrences (all) | 3 | 3 |
| Hyperglycaemia | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 37 (5.41%) |
| occurrences (all) | 0 | 3 |
| Hyperkalaemia | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 37 (0.00%) |
| occurrences (all) | 2 | 0 |
| Hypomagnesaemia | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 6 / 37 (16.22%) |
| occurrences (all) | 3 | 10 |
| Hypophosphataemia | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 37 (5.41%) |
| occurrences (all) | 1 | 2 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 02 January 2014 | The primary purpose of the amendment was to clarify the designation of study visits: Cycles where both pemetrexed and cisplatin were given were designated TCycles. Cycles where maintenance pemetrexed was given were designated MCycles. Ruxolitinib or placebo were given during both TCycles and MCycles |
| 01 July 2014 | The primary purpose of the amendment was to revise requirements regarding prior treatments and to clarify language referring to pleural/pericardial effusion. The clinically important changes included: <ul style="list-style-type: none">• Revision of the requirement for wash-out for prior treatments of central nervous system metastases• Removal of language referring to pleural/pericardial effusion as a descriptor for Stage IIIB NCSLC. |
| 10 September 2014 | The primary purpose of the amendment was to add or clarify several items. The clinically important changes included: <ul style="list-style-type: none">• Addition of an additional exclusion criteria of prior JAK inhibitor use• Addition of a risks summary for granulocyte colony-stimulating factor (GCSF)• Addition of additional information on the DMC• Update to information regarding contraceptive use• Addition of a listing of inducers of CYP 3A4. |
| 02 February 2015 | The primary purpose of the amendment was to add or clarify several items. The clinically important changes included: <ul style="list-style-type: none">• Addition of a brief summary of Part 1 and to designate the dose for Part 2 as 15 mg BID ruxolitinib/matching placebo, without prophylactic GCSF in a randomized, double-blind comparison• Removal of language describing prophylactic GCSF use and the possibility for open label study for clarity• Addition of a prescreening C-reactive protein measurement and an optional tissue biopsy for consenting subjects• Update to contraceptive language• Addition of options for administration of vitamin B12• Addition of options for use of dexamethasone as both an anti-inflammatory and anti emetic prophylaxis. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|---|--------------|
| 11 February 2016 | The study was terminated as other related studies of ruxolitinib did not provide sufficient efficacy to warrant continuation. | - |

Notes:

Limitations and caveats

None reported