



## Clinical trial results:

### An Open-Label, Randomized, Phase 2 Dose-Finding Study of Pacritinib in Patients with Primary Myelofibrosis, Post-Polycythemia Vera Myelofibrosis, or Post-Essential Thrombocythemia Myelofibrosis Previously Treated with Ruxolitinib

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2017-001772-28    |
| Trial protocol           | GB HU SE ES FR IT |
| Global end of trial date | 04 September 2019 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 19 December 2020 |
| First version publication date | 19 December 2020 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | PAC203 |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | CTI BioPharma Corp   |
| Sponsor organisation address | 3101 Western Ave, Seattle, United States, 98121  |
| Public contact               | Regulatory Affairs-Sarah H. Telzrow, CTI BioPharma Corp., +1 2062724426, stelzrow@ctibiopharma.com |
| Scientific contact           | Regulatory Affairs-Sarah H. Telzrow, CTI BioPharma Corp., +1 2062724426, stelzrow@ctibiopharma.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                                       | Interim           |
| Date of interim/final analysis                       | 17 December 2018  |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 16 November 2018  |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 04 September 2019 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to explore the dose-response relationship for pacritinib among primary and secondary myelofibrosis (MF) patients to determine a recommended dosage for further clinical studies.

Protection of trial subjects:

The described study was performed in compliance with the Declaration of Helsinki, ICH guidelines, US Food and Drug Administration (FDA) regulations 21 CFR Parts 50, 56, and 312, and with the laws and regulations of the country in which the research was conducted, whichever afforded the greatest protection to the study patient.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 26 June 2017 |
| Long term follow-up planned                               | Yes          |
| Long term follow-up rationale                             | Safety       |
| Long term follow-up duration                              | 30 Months    |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Spain: 6           |
| Country: Number of subjects enrolled | Sweden: 1          |
| Country: Number of subjects enrolled | United Kingdom: 20 |
| Country: Number of subjects enrolled | France: 10         |
| Country: Number of subjects enrolled | Hungary: 10        |
| Country: Number of subjects enrolled | Italy: 7           |
| Country: Number of subjects enrolled | United States: 111 |
| Worldwide total number of subjects   | 165                |
| EEA total number of subjects         | 54                 |

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)                     | 44  |
| From 65 to 84 years                      | 118 |
| 85 years and over                        | 3   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Screening procedures were completed between Days -35 and -7, before treatment initiation with the exception of the Screening (Baseline) MRI or CT scan, which was performed between Days -10 and -4.

### Period 1

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

### Arms

|                              |                      |
|------------------------------|----------------------|
| Are arms mutually exclusive? | Yes                  |
| <b>Arm title</b>             | Pacritinib 100 mg QD |

Arm description:

Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy.

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

Dosage and administration details:

Pacritinib 100 mg (1 capsule) once daily (QD) orally, at the same time of day, with or without food during 24 weeks.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Pacritinib 100 mg BID |
|------------------|-----------------------|

Arm description:

Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy.

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

Dosage and administration details:

Pacritinib 100 mg (1 capsule) twice daily (BID) orally, at the same time of day, with or without food during 24 weeks.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Pacritinib 200 mg BID |
|------------------|-----------------------|

Arm description:

Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy.

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

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

Dosage and administration details:

Pacritinib 200 mg (2 capsule) BID orally, at the same time of day, with or without food during 24 weeks.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Pacritinib 100 mg QD | Pacritinib 100 mg BID | Pacritinib 200 mg BID |
|---|----------------------|-----------------------|-----------------------|
| Started   | 52                   | 55                    | 54                    |
| Completed   | 5                    | 9                     | 8                     |
| Not completed                                       | 47                   | 46                    | 46                    |
| Adverse event, serious fatal                        | 4                    | 3                     | 3                     |
| Consent withdrawn by subject                        | 11                   | 7                     | 6                     |
| Physician decision                                  | 23                   | 17                    | 23                    |
| Adverse event, non-fatal                            | 2                    | 8                     | 7                     |
| Study Terminated By Sponsor                         | 5                    | 7                     | 5                     |
| Death   | 1                    | 1                     | -                     |
| Other   | 1                    | 3                     | 1                     |
| Lost to follow-up                                   | -                    | -                     | 1                     |

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: A total of 165 were randomized in the trial, but only 161 subjects were included in the Full Analysis Population (FAP), this included all subjects who received at least 1 dose of study drug and had any efficacy measurements.

The discontinuations reasons are treated related only.

## Baseline characteristics

### Reporting groups

|   |                       |
|---|-----------------------|
| Reporting group title   | Pacritinib 100 mg QD  |
| Reporting group description:<br>Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy. |                       |
| Reporting group title   | Pacritinib 100 mg BID |
| Reporting group description:<br>Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy. |                       |
| Reporting group title   | Pacritinib 200 mg BID |
| Reporting group description:<br>Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy. |                       |

| Reporting group values  | Pacritinib 100 mg QD | Pacritinib 100 mg BID | Pacritinib 200 mg BID |
|---|----------------------|-----------------------|-----------------------|
| Number of subjects  | 52                   | 55                    | 54                    |
| Age categorical   |                      |                       |                       |
| The full analysis set (FAS) was defined as all randomized patients who received at least 1 dose of study drug. Patients in this population were analyzed according to the treatment group to which they were assigned at randomization. |                      |                       |                       |
| 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)  | 16                   | 11                    | 16                    |
| From 65-84 years  | 34                   | 44                    | 37                    |
| 85 years and over   | 2                    | 0                     | 1                     |
| Gender categorical  |                      |                       |                       |
| Units: Subjects   |                      |                       |                       |
| Female  | 21                   | 26                    | 22                    |
| Male  | 31                   | 29                    | 32                    |

| Reporting group values  | Total |  |  |
|---|-------|--|--|
| Number of subjects  | 161   |  |  |
| Age categorical   |       |  |  |
| The full analysis set (FAS) was defined as all randomized patients who received at least 1 dose of study drug. Patients in this population were analyzed according to the treatment group to which they were assigned at randomization. |       |  |  |
| Units: Subjects   |       |  |  |
| In utero  | 0     |  |  |
| Preterm newborn infants (gestational age < 37 wks)  | 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)      | 43  |  |  |
| From 65-84 years          | 115 |  |  |
| 85 years and over         | 3   |  |  |
| Gender categorical        |     |  |  |
| Units: Subjects           |     |  |  |
| Female                    | 69  |  |  |
| Male                      | 92  |  |  |

## End points

### End points reporting groups

|   |                       |
|---|-----------------------|
| Reporting group title   | Pacritinib 100 mg QD  |
| Reporting group description:<br>Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy. |                       |
| Reporting group title   | Pacritinib 100 mg BID |
| Reporting group description:<br>Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy. |                       |
| Reporting group title   | Pacritinib 200 mg BID |
| Reporting group description:<br>Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy. |                       |

### Primary: Percent Reduction in Spleen Volume at Weeks 12 and 24

|  |   |
|--|---|
| End point title  | Percent Reduction in Spleen Volume at Weeks 12 and 24 |
| End point description:<br>The primary efficacy endpoint of this study was the percent reduction in spleen volume from baseline as measured by magnetic resonance imaging (MRI) or computed tomography (CT) at Weeks 12 and 24. Spleen volume at End of Treatment (EOT) was defined as the spleen volume collected at the EOT visit or the last spleen volume measured on treatment if not measured at EOT. |   |
| End point type   | Primary   |
| End point timeframe:<br>The primary efficacy endpoint was examined from baseline at Weeks 12, 24 and at EOT.   |   |

| End point values            | Pacritinib 100 mg QD | Pacritinib 100 mg BID | Pacritinib 200 mg BID |  |
|-----------------------------|----------------------|-----------------------|-----------------------|--|
| Subject group type          | Reporting group      | Reporting group       | Reporting group       |  |
| Number of subjects analysed | 52                   | 55                    | 54                    |  |
| Units: Subjects             | 52                   | 55                    | 54                    |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Spleen volume reduction ( $\geq 35\%$ ) - 100mg QD                   |
| Comparison groups                       | Pacritinib 100 mg BID v Pacritinib 100 mg QD v Pacritinib 200 mg BID |
| Number of subjects included in analysis | 161  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other <sup>[1]</sup>   |
| Parameter estimate                      | Descriptive statistics - Percentages                                 |
| Point estimate                          | 0  |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0       |
| upper limit         | 6.8     |

Notes:

[1] - Statistical programming and analyses were performed using SAS® version 9.4.

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Spleen volume reduction ( $\geq 35\%$ ) - 100mg BID |
|-----------------------------------|---|

Statistical analysis description:

To examine the dose-response relationship for efficacy, as measured by SVR using MRI (preferred) or CT and TSS using the MPN-SAF TSS 2.0

|   |  |
|---|--|
| Comparison groups                       | Pacritinib 100 mg BID v Pacritinib 100 mg QD v Pacritinib 200 mg BID |
| Number of subjects included in analysis | 161  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other  |
| Parameter estimate                      | Descriptive statistics - Percentages                                 |
| Point estimate                          | 1.8  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0  |
| upper limit                             | 9.7  |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Spleen volume reduction ( $\geq 35\%$ ) - 200mg BID                  |
| Comparison groups                       | Pacritinib 100 mg QD v Pacritinib 100 mg BID v Pacritinib 200 mg BID |
| Number of subjects included in analysis | 161  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other  |
| Parameter estimate                      | Descriptive statistics - Percentages                                 |
| Point estimate                          | 9.3  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 3.1  |
| upper limit                             | 20.3   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected during the clinical study from the time the patient signed the informed consent through 30 days following last dose of study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Pacritinib 100 mg QD |
|-----------------------|----------------------|

Reporting group description:

Patients with primary or secondary MF (Dynamic International Prognostic Scoring System [DIPSS] risk score of Intermediate-1 to High-Risk) who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy.

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Pacritinib 100 mg BID |
|-----------------------|-----------------------|

Reporting group description:

Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy.

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Pacritinib 200 mg BID |
|-----------------------|-----------------------|

Reporting group description:

Patients with primary or secondary MF who were previously treated with ruxolitinib. Patients included in this study previously failed therapy with ruxolitinib on the basis of intolerance or lack of efficacy.

| Serious adverse events  | Pacritinib 100 mg QD | Pacritinib 100 mg BID | Pacritinib 200 mg BID |
|---|----------------------|-----------------------|-----------------------|
| Total subjects affected by serious adverse events                   |                      |                       |                       |
| subjects affected / exposed   | 19 / 52 (36.54%)     | 20 / 55 (36.36%)      | 25 / 54 (46.30%)      |
| number of deaths (all causes)                                       | 6                    | 4                     | 5                     |
| number of deaths resulting from adverse events                      | 3                    | 2                     | 3                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                      |                       |                       |
| Malignant melanoma in situ  |                      |                       |                       |
| subjects affected / exposed   | 0 / 52 (0.00%)       | 1 / 55 (1.82%)        | 0 / 54 (0.00%)        |
| occurrences causally related to treatment / all                     | 0 / 0                | 0 / 1                 | 0 / 0                 |
| deaths causally related to treatment / all                          | 0 / 0                | 0 / 0                 | 0 / 0                 |
| Malignant pleural effusion  |                      |                       |                       |
| subjects affected / exposed   | 0 / 52 (0.00%)       | 1 / 55 (1.82%)        | 0 / 54 (0.00%)        |
| occurrences causally related to treatment / all                     | 0 / 0                | 0 / 1                 | 0 / 0                 |
| deaths causally related to treatment / all                          | 0 / 0                | 0 / 0                 | 0 / 0                 |
| Myeloproliferative disorder   |                      |                       |                       |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 1          | 0 / 0          |
| Pituitary tumour benign                              |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Prostate cancer                                      |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                                   |                |                |                |
| Haematoma  |                |                |                |
| subjects affected / exposed                          | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular compression                                 |                |                |                |
| subjects affected / exposed                          | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension  |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Pyrexia  |                |                |                |
| subjects affected / exposed                          | 3 / 52 (5.77%) | 2 / 55 (3.64%) | 3 / 54 (5.56%) |
| occurrences causally related to treatment / all      | 1 / 3          | 1 / 2          | 0 / 3          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General physical health deterioration                |                |                |                |
| subjects affected / exposed                          | 2 / 52 (3.85%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 3          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Disease progression                             |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Drug withdrawal syndrome                        |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oedema peripheral                               |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Asthenia  |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                          |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 2 / 55 (3.64%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Epistaxis                                       |                |                |                |
| subjects affected / exposed                     | 2 / 52 (3.85%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lung infiltration                               |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Hypoxia   |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory distress                            |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory failure                             |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Investigations                                  |                |                |                |
| Blood bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ejection fraction decreased                     |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Troponin increased                              |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Subdural haematoma                              |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Transfusion reaction                            |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Delayed haemolytic transfusion reaction         |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Incorrect drug administration duration          |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Subdural haemorrhage                            |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Pericardial effusion                            |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Arrhythmia supraventricular                     |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial fibrillation                             |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Optic neuritis                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope   |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Headache  |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Febrile neutropenia                             |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lymphadenopathy                                 |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Splenic infarction                              |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Thrombocytopenia                                |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Thrombocytosis                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |                |                |                |
| Colitis   |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Large intestinal obstruction                    |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ascites   |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal haemorrhage                    |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 2 / 54 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intestinal obstruction                          |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Renal and urinary disorders</b>              |                |                |                |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal failure acute                             |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 2 / 54 (3.70%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Calculus ureteric                               |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hydronephrosis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal impairment                                |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal mass                                      |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Bone pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Muscle haemorrhage                              |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 2 / 52 (3.85%) | 2 / 55 (3.64%) | 5 / 54 (9.26%) |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 2          | 1 / 5          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post procedural infection                       |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 1 / 55 (1.82%) | 2 / 54 (3.70%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1          |
| Tuberculosis                                    |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 2 / 55 (3.64%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abscess limb                                    |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchitis                                      |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clostridium difficile colitis                   |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 2 / 54 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 2 / 54 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Herpes oesophagitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Influenza                                       |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lower respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Soft tissue infection                           |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tooth abscess                                   |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 55 (1.82%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Hyperuricaemia                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 55 (0.00%) | 0 / 54 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 3 / 55 (5.45%) | 2 / 54 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 4          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fluid overload                                  |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypokalaemia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                                   | Pacritinib 100 mg QD | Pacritinib 100 mg BID | Pacritinib 200 mg BID |
|---|----------------------|-----------------------|-----------------------|
| Total subjects affected by non-serious adverse events               |                      |                       |                       |
| subjects affected / exposed   | 47 / 52 (90.38%)     | 51 / 55 (92.73%)      | 54 / 54 (100.00%)     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                      |                       |                       |
| Basal cell carcinoma  |                      |                       |                       |
| subjects affected / exposed   | 3 / 52 (5.77%)       | 1 / 55 (1.82%)        | 0 / 54 (0.00%)        |
| occurrences (all)   | 3                    | 1                     | 0                     |
| Vascular disorders  |                      |                       |                       |
| Haematoma   |                      |                       |                       |
| subjects affected / exposed   | 3 / 52 (5.77%)       | 0 / 55 (0.00%)        | 1 / 54 (1.85%)        |
| occurrences (all)   | 3                    | 0                     | 1                     |
| Hypertension  |                      |                       |                       |
| subjects affected / exposed   | 0 / 52 (0.00%)       | 3 / 55 (5.45%)        | 2 / 54 (3.70%)        |
| occurrences (all)   | 0                    | 4                     | 2                     |
| General disorders and administration site conditions                |                      |                       |                       |

|   |                 |                  |                  |
|---|-----------------|------------------|------------------|
| Fatigue   |                 |                  |                  |
| subjects affected / exposed                     | 9 / 52 (17.31%) | 13 / 55 (23.64%) | 13 / 54 (24.07%) |
| occurrences (all)                               | 11              | 17               | 15               |
| Oedema peripheral                               |                 |                  |                  |
| subjects affected / exposed                     | 6 / 52 (11.54%) | 5 / 55 (9.09%)   | 9 / 54 (16.67%)  |
| occurrences (all)                               | 7               | 5                | 11               |
| Pyrexia   |                 |                  |                  |
| subjects affected / exposed                     | 6 / 52 (11.54%) | 8 / 55 (14.55%)  | 5 / 54 (9.26%)   |
| occurrences (all)                               | 6               | 8                | 5                |
| Chills  |                 |                  |                  |
| subjects affected / exposed                     | 5 / 52 (9.62%)  | 2 / 55 (3.64%)   | 4 / 54 (7.41%)   |
| occurrences (all)                               | 5               | 2                | 4                |
| Non-cardiac chest pain                          |                 |                  |                  |
| subjects affected / exposed                     | 3 / 52 (5.77%)  | 2 / 55 (3.64%)   | 0 / 54 (0.00%)   |
| occurrences (all)                               | 3               | 2                | 0                |
| Early satiety                                   |                 |                  |                  |
| subjects affected / exposed                     | 0 / 52 (0.00%)  | 1 / 55 (1.82%)   | 3 / 54 (5.56%)   |
| occurrences (all)                               | 0               | 1                | 3                |
| Respiratory, thoracic and mediastinal disorders |                 |                  |                  |
| Cough   |                 |                  |                  |
| subjects affected / exposed                     | 5 / 52 (9.62%)  | 5 / 55 (9.09%)   | 6 / 54 (11.11%)  |
| occurrences (all)                               | 8               | 6                | 6                |
| Epistaxis                                       |                 |                  |                  |
| subjects affected / exposed                     | 3 / 52 (5.77%)  | 4 / 55 (7.27%)   | 8 / 54 (14.81%)  |
| occurrences (all)                               | 3               | 6                | 13               |
| Dyspnoea  |                 |                  |                  |
| subjects affected / exposed                     | 2 / 52 (3.85%)  | 7 / 55 (12.73%)  | 6 / 54 (11.11%)  |
| occurrences (all)                               | 2               | 8                | 7                |
| Pleural effusion                                |                 |                  |                  |
| subjects affected / exposed                     | 1 / 52 (1.92%)  | 2 / 55 (3.64%)   | 4 / 54 (7.41%)   |
| occurrences (all)                               | 1               | 2                | 4                |
| Psychiatric disorders                           |                 |                  |                  |
| Insomnia  |                 |                  |                  |
| subjects affected / exposed                     | 3 / 52 (5.77%)  | 3 / 55 (5.45%)   | 7 / 54 (12.96%)  |
| occurrences (all)                               | 3               | 3                | 8                |
| Investigations                                  |                 |                  |                  |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                        | 4 / 52 (7.69%)<br>4 | 1 / 55 (1.82%)<br>1 | 3 / 54 (5.56%)<br>5 |
| Blood creatine increased<br>subjects affected / exposed<br>occurrences (all)                | 3 / 52 (5.77%)<br>3 | 2 / 55 (3.64%)<br>2 | 2 / 54 (3.70%)<br>2 |
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)          | 3 / 52 (5.77%)<br>4 | 2 / 55 (3.64%)<br>2 | 4 / 54 (7.41%)<br>4 |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)                | 3 / 52 (5.77%)<br>3 | 3 / 55 (5.45%)<br>4 | 3 / 54 (5.56%)<br>5 |
| Ejection fraction decreased<br>subjects affected / exposed<br>occurrences (all)             | 2 / 52 (3.85%)<br>3 | 3 / 55 (5.45%)<br>5 | 2 / 54 (3.70%)<br>2 |
| Aspartate aminotransferase<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 52 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 | 3 / 54 (5.56%)<br>3 |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)        | 0 / 52 (0.00%)<br>0 | 3 / 55 (5.45%)<br>4 | 3 / 54 (5.56%)<br>5 |
| Injury, poisoning and procedural<br>complications   |                     |                     |                     |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                               | 5 / 52 (9.62%)<br>5 | 2 / 55 (3.64%)<br>3 | 5 / 54 (9.26%)<br>7 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                    | 4 / 52 (7.69%)<br>4 | 0 / 55 (0.00%)<br>0 | 1 / 54 (1.85%)<br>1 |
| Nervous system disorders  |                     |                     |                     |
| Memory impairment<br>subjects affected / exposed<br>occurrences (all)                       | 3 / 52 (5.77%)<br>3 | 0 / 55 (0.00%)<br>0 | 0 / 54 (0.00%)<br>0 |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)                            | 3 / 52 (5.77%)<br>3 | 2 / 55 (3.64%)<br>2 | 1 / 54 (1.85%)<br>1 |
| Dizziness   |                     |                     |                     |

|  |                        |                        |                        |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                     | 2 / 52 (3.85%)<br>2    | 2 / 55 (3.64%)<br>2    | 5 / 54 (9.26%)<br>5    |
| Headache<br>subjects affected / exposed<br>occurrences (all)         | 2 / 52 (3.85%)<br>2    | 5 / 55 (9.09%)<br>5    | 2 / 54 (3.70%)<br>2    |
| Blood and lymphatic system disorders                                 |                        |                        |                        |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all) | 8 / 52 (15.38%)<br>13  | 8 / 55 (14.55%)<br>10  | 19 / 54 (35.19%)<br>31 |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)          | 5 / 52 (9.62%)<br>5    | 5 / 55 (9.09%)<br>7    | 13 / 54 (24.07%)<br>19 |
| Leukocytosis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 52 (0.00%)<br>0    | 3 / 55 (5.45%)<br>3    | 0 / 54 (0.00%)<br>0    |
| Gastrointestinal disorders   |                        |                        |                        |
| Nausea<br>subjects affected / exposed<br>occurrences (all)           | 12 / 52 (23.08%)<br>12 | 11 / 55 (20.00%)<br>12 | 15 / 54 (27.78%)<br>15 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)        | 10 / 52 (19.23%)<br>14 | 12 / 55 (21.82%)<br>14 | 16 / 54 (29.63%)<br>26 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)   | 9 / 52 (17.31%)<br>11  | 6 / 55 (10.91%)<br>6   | 13 / 54 (24.07%)<br>15 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)         | 3 / 52 (5.77%)<br>3    | 2 / 55 (3.64%)<br>2    | 8 / 54 (14.81%)<br>8   |
| Constipation<br>subjects affected / exposed<br>occurrences (all)     | 2 / 52 (3.85%)<br>2    | 1 / 55 (1.82%)<br>1    | 10 / 54 (18.52%)<br>10 |
| Skin and subcutaneous tissue disorders                               |                        |                        |                        |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)     | 3 / 52 (5.77%)<br>3    | 1 / 55 (1.82%)<br>1    | 4 / 54 (7.41%)<br>5    |
| Petechiae  |                        |                        |                        |

|   |                      |                        |                        |
|---|----------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)  | 3 / 52 (5.77%)<br>3  | 2 / 55 (3.64%)<br>2    | 4 / 54 (7.41%)<br>5    |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 2 / 52 (3.85%)<br>2  | 10 / 55 (18.18%)<br>12 | 6 / 54 (11.11%)<br>6   |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 2 / 52 (3.85%)<br>2  | 3 / 55 (5.45%)<br>5    | 3 / 54 (5.56%)<br>3    |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 52 (1.92%)<br>1  | 1 / 55 (1.82%)<br>1    | 4 / 54 (7.41%)<br>4    |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 4 / 52 (7.69%)<br>5  | 1 / 55 (1.82%)<br>1    | 5 / 54 (9.26%)<br>5    |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 2 / 52 (3.85%)<br>2  | 3 / 55 (5.45%)<br>3    | 5 / 54 (9.26%)<br>5    |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 2 / 52 (3.85%)<br>2  | 3 / 55 (5.45%)<br>3    | 3 / 54 (5.56%)<br>3    |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 52 (1.92%)<br>1  | 3 / 55 (5.45%)<br>3    | 0 / 54 (0.00%)<br>0    |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 52 (7.69%)<br>7  | 3 / 55 (5.45%)<br>3    | 1 / 54 (1.85%)<br>1    |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 52 (1.92%)<br>1  | 1 / 55 (1.82%)<br>1    | 3 / 54 (5.56%)<br>4    |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all)      | 6 / 52 (11.54%)<br>6 | 4 / 55 (7.27%)<br>7    | 10 / 54 (18.52%)<br>11 |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Fluid overload              |                |                |                |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 55 (0.00%) | 5 / 54 (9.26%) |
| occurrences (all)           | 0              | 0              | 5              |
| Gout                        |                |                |                |
| subjects affected / exposed | 0 / 52 (0.00%) | 3 / 55 (5.45%) | 4 / 54 (7.41%) |
| occurrences (all)           | 0              | 5              | 6              |
| Hyperuricaemia              |                |                |                |
| subjects affected / exposed | 0 / 52 (0.00%) | 2 / 55 (3.64%) | 3 / 54 (5.56%) |
| occurrences (all)           | 0              | 2              | 4              |
| Hyponatraemia               |                |                |                |
| subjects affected / exposed | 0 / 52 (0.00%) | 3 / 55 (5.45%) | 3 / 54 (5.56%) |
| occurrences (all)           | 0              | 4              | 3              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 08 November 2017  | <ul style="list-style-type: none"><li>•Timing changed for the first interim analysis to minimize treatment of patients with an ineffective dose</li><li>•Randomization stratified by baseline platelet count &amp; geographic region to ensure balance in risk factors between study arms</li><li>•DNA samples collection to be used in future analyses to determine if specific mutations predict responsiveness to pacritinib</li><li>• Screening visit window modified to support the investigator &amp; site staff in the scheduling &amp; performing of tests &amp; assessments</li><li>•Included additional changes required by the French,United Kingdom,Swedish &amp; German regulatory bodies</li><li>•Inclusion criteria changed to ensure that patients who enter the study had a documented adequate trial on ruxolitinib without demonstrated substantial efficacy</li><li>•Revised text to define symptom control failure by the TSS instrument &amp; ensure that only patients without adequate symptom control are eligible</li><li>•Concomitant use of growth factor therapy prohibited</li><li>•Corticosteroids to be used as supportive care for medically indicated conditions</li><li>•Deleted dose re-escalation language as PAC203 is a dose-finding study</li><li>•Added hemoglobin A1C &amp; high sensitivity CRP tests to central laboratory analysis for future use as pharmacodynamics markers for pacritinib</li><li>•Added modifications to specify that all prior experimental therapy requires a 28-day washout prior to randomization to ensure that drug associated AEs from prior therapy are identified &amp; reported</li><li>•Allowed patients to continue pacritinib after 24 weeks &amp; define follow up assessments as evaluation of long-term safety of pacritinib is a secondary goal of the study</li><li>•Deleted platelet count inclusion criterion to eliminate an impediment to enrollment not been shown to be associated with safety concerns</li><li>•Added timing details for subsequent interim analyses to the first interim one</li><li>•Deleted pacritinib dose reduction for patients requiring antiplatelet or anticoagulation agent to treat AEs</li><li>•Allowed patients with platelets <math>\geq 100,000/\mu\text{L}</math></li></ul> |
| 16 April 2018     | <ul style="list-style-type: none"><li>• Expanded sample size to approximately 150 patients (up to 50 patients/arm)</li><li>• Included additional dense PK blood sampling at selected sites for approximately 6 to 8 patients per treatment group</li><li>• Specified a 30-minute window for the 0-hour (predose) PK &amp; pharmacodynamics blood sampling</li><li>• Specified that samples collected for unscheduled hematology &amp; serum chemistry tests may be analyzed locally but must also be submitted to the central laboratory for testing &amp; entry into the EDC</li><li>• Excluded patients on high-dose ruxolitinib (more than 10 mg BID or 20 mg QD) who cannot tolerate tapering off ruxolitinib prior to the first dose of pacritinib</li><li>• Removed the requirement for central radiographic confirmation of disease progression prior to stopping treatment</li></ul>  |
| 14 September 2018 | <ul style="list-style-type: none"><li>• Revised study design to remove BPP interim futility analyses</li><li>• Added text to require that if a grade 4 thrombocytopenia recurs after restarting drug, pacritinib must be discontinued per request from the French Competent Authority</li></ul>   |

|             |   |
|-------------|---|
| 06 May 2019 | <ul style="list-style-type: none"> <li>• Revised study design to terminate pacritinib treatment &amp; study assessments at and beyond the Week 24 timepoint to conclude Phase 2 dose-finding study in preparation for Phase 3</li> <li>• Added provision allowing patients who are benefiting from therapy, as of study drug termination, to continue receiving pacritinib under single patient expanded access or named patient programs at investigator discretion &amp; subject to regulatory and IEC/IRB approval</li> <li>• Clarified that the FAS is defined as all randomized patients who received at least one dose of study drug. Remove reference to "Per Protocol Population."</li> </ul> |
|-------------|---|

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported