



## Clinical trial results:

### Multicenter, Open-Label, Single Arm, Phase II Exploratory Study to Evaluate the Effect of a One-Year Consolidation Treatment with Ponatinib 15 mg on Treatment Free-Remission Rate in Patients with Philadelphia-Positive Chronic Myeloid Leukemia, who had previously Achieved a Deep Molecular Response with Imatinib

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-004565-27 |
| Trial protocol           | ES             |
| Global end of trial date | 29 April 2024  |

#### Results information

|                                   |                                                                    |
|-----------------------------------|--------------------------------------------------------------------|
| Result version number             | v1 (current)                                                       |
| This version publication date     | 11 April 2025                                                      |
| First version publication date    | 11 April 2025                                                      |
| Summary attachment (see zip file) | PonaZero_Resumen Resultados (PonaZero_Resumen Resultados_REec.pdf) |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | PonaZero_study |
|-----------------------|----------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                                           |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | FUNDACIÓN TEÓFILO HERNANDO                                                                                                |
| Sponsor organisation address | Edificio las Rozas 23, planta S, oficina 1, Ctra. de La Coruña, km 23, 200, 28290 Las Rozas de Madr, Madrid, Spain, 28290 |
| Public contact               | Cecilia López García, FUNDACIÓN TEÓFILO HERNANDO, 0034 911923700, coordinacion.clinica@ifth.es                            |
| Scientific contact           | Cecilia López García, FUNDACIÓN TEÓFILO HERNANDO, 0034 911923700, coordinacion.clinica@ifth.es                            |

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                       | 20 August 2024 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 07 June 2023   |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 29 April 2024  |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to evaluate the proportion of patients without confirmed loss of MR4 or loss of MMR (don't require confirmation) within 48 weeks following ponatinib therapy cessation.

Protection of trial subjects:

1. The protocol and the informed consent were review and approved by the IEC of the Hospital Universitario de la Princesa (10/10/2018) and the AEMPS (15/11/2018).
2. Patients gave informed consent before the study began.
3. The clinical trials was conducted in accordance with the Declaration of Helsinki, GCP, and applicable regulatory requirements
4. The CRAs in charge of the trial periodically monitored that the study was conducted in accordance with the protocol and verified the accuracy and completeness of the data recorded in the eCRFs.
5. All patient information in this clinical trial was handled with the highest level of confidentiality. Patients were assigned a unique coded identifier (XX-XX) instead of using personal names to ensure their anonymity. This coding system was applied to all study-related documentation, including eCRFs, laboratory reports, and study databases.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 25 June 2019     |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 2 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 24 |
| Worldwide total number of subjects   | 24        |
| EEA total number of subjects         | 24        |

Notes:

### Subjects enrolled per age group

|                                           |   |
|-------------------------------------------|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |

|                                          |    |
|------------------------------------------|----|
| Infants and toddlers (28 days-23 months) | 0  |
| Children (2-11 years)                    | 0  |
| Adolescents (12-17 years)                | 0  |
| Adults (18-64 years)                     | 20 |
| From 65 to 84 years                      | 4  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment start date: 25/06/2019

Recruitment end date: 16/07/2021

Number of centers: 8

Patients recruited: 24 (center 2= 3; center 3= 1; center 4= 9; center 6= 1; center 8= 1, center 9= 4; center 10= 1; center 11= 4)

### Pre-assignment

Screening details:

Number of subjects screened: 24

Number of screening failures: 1 did not meet the inclusion criteria (center 11)

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Consolidation phase (48 weeks) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |            |
|-----------|------------|
| Arm title | Single-arm |
|-----------|------------|

Arm description:

Patients that received ponatinib 15 mg during the consolidation phase

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Ponatinib          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

15 mg once daily

| Number of subjects in period 1 <sup>[1]</sup> | Single-arm |
|-----------------------------------------------|------------|
| Started                                       | 23         |
| Consolidation phase                           | 23         |
| Completed                                     | 19         |
| Not completed                                 | 4          |
| Adverse event, non-fatal                      | 3          |
| Protocol deviation                            | 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: In total, 24 patients were enrolled and 23 were included in the study as 1 patients was a screening failure.

|                                                           |                                     |
|-----------------------------------------------------------|-------------------------------------|
| <b>Period 2</b>                                           |                                     |
| Period 2 title                                            | Treatment-Free Remission (96 weeks) |
| Is this the baseline period?                              | No                                  |
| Allocation method                                         | Not applicable                      |
| Blinding used                                             | Not blinded                         |
| <b>Arms</b>                                               |                                     |
| <b>Arm title</b>                                          | Single-arm                          |
| Arm description: -                                        |                                     |
| Arm type                                                  | No intervention                     |
| No investigational medicinal product assigned in this arm |                                     |

| <b>Number of subjects in period 2</b> | Single-arm |
|---------------------------------------|------------|
| Started                               | 19         |
| Completed                             | 13         |
| Not completed                         | 6          |
| Loss of molecular response            | 6          |

## Baseline characteristics

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Consolidation phase (48 weeks) |
|-----------------------|--------------------------------|

Reporting group description: -

| Reporting group values                                | Consolidation phase<br>(48 weeks) | Total |  |
|-------------------------------------------------------|-----------------------------------|-------|--|
| Number of subjects                                    | 23                                | 23    |  |
| Age categorical<br>Units: Subjects                    |                                   |       |  |
| In utero                                              | 0                                 | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                                 | 0     |  |
| Newborns (0-27 days)                                  | 0                                 | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0                                 | 0     |  |
| Children (2-11 years)                                 | 0                                 | 0     |  |
| Adolescents (12-17 years)                             | 0                                 | 0     |  |
| Adults (18-64 years)                                  | 19                                | 19    |  |
| From 65-84 years                                      | 4                                 | 4     |  |
| 85 years and over                                     | 0                                 | 0     |  |
| Age continuous<br>Units: years                        |                                   |       |  |
| arithmetic mean                                       | 52.8                              |       |  |
| standard deviation                                    | ± 14.1                            | -     |  |
| Gender categorical<br>Units: Subjects                 |                                   |       |  |
| Female                                                | 8                                 | 8     |  |
| Male                                                  | 15                                | 15    |  |
| Race<br>Units: Subjects                               |                                   |       |  |
| Caucasian                                             | 22                                | 22    |  |
| Latin                                                 | 1                                 | 1     |  |
| ECOG<br>Units: Subjects                               |                                   |       |  |
| 0-zero                                                | 19                                | 19    |  |
| 1-one                                                 | 4                                 | 4     |  |
| Physical examination - General<br>Units: Subjects     |                                   |       |  |
| Normal                                                | 22                                | 22    |  |
| Abnormal                                              | 1                                 | 1     |  |
| Physical examination - Skin<br>Units: Subjects        |                                   |       |  |
| Normal                                                | 22                                | 22    |  |
| Abnormal                                              | 1                                 | 1     |  |
| Physical examination - Neck<br>Units: Subjects        |                                   |       |  |
| Normal                                                | 23                                | 23    |  |
| Abnormal                                              | 0                                 | 0     |  |

|                                                        |    |    |  |
|--------------------------------------------------------|----|----|--|
| Physical examination - Ears<br>Units: Subjects         |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Eyes<br>Units: Subjects         |    |    |  |
| Normal                                                 | 22 | 22 |  |
| Abnormal                                               | 1  | 1  |  |
| Physical examination - Nose<br>Units: Subjects         |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Heart<br>Units: Subjects        |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Throat<br>Units: Subjects       |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Lungs<br>Units: Subjects        |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Abdomen<br>Units: Subjects      |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Back<br>Units: Subjects         |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Lymph nodes<br>Units: Subjects  |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Neurologic<br>Units: Subjects   |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Extremities<br>Units: Subjects  |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Vascular<br>Units: Subjects     |    |    |  |
| Normal                                                 | 23 | 23 |  |
| Abnormal                                               | 0  | 0  |  |
| Physical examination - Extramedular<br>Units: Subjects |    |    |  |
| Normal                                                 | 23 | 23 |  |

|                                                 |        |    |  |
|-------------------------------------------------|--------|----|--|
| Abnormal                                        | 0      | 0  |  |
| Electrocardiogram<br>Units: Subjects            |        |    |  |
| Normal                                          | 22     | 22 |  |
| Abnormal                                        | 1      | 1  |  |
| Echocardiogram<br>Units: Subjects               |        |    |  |
| Normal                                          | 21     | 21 |  |
| Abnormal                                        | 2      | 2  |  |
| Pregnancy test<br>Units: Subjects               |        |    |  |
| Negative                                        | 3      | 3  |  |
| Not applicable                                  | 20     | 20 |  |
| Hepatitis B surface antibody<br>Units: Subjects |        |    |  |
| Negative                                        | 15     | 15 |  |
| Positive                                        | 6      | 6  |  |
| No data                                         | 2      | 2  |  |
| Hepatitis B surface antigen<br>Units: Subjects  |        |    |  |
| Negative                                        | 21     | 21 |  |
| Positive                                        | 0      | 0  |  |
| No data                                         | 2      | 2  |  |
| Hepatitis B core<br>Units: Subjects             |        |    |  |
| Negative                                        | 19     | 19 |  |
| Positive                                        | 2      | 2  |  |
| No data                                         | 2      | 2  |  |
| Height<br>Units: cm                             |        |    |  |
| arithmetic mean                                 | 167.4  |    |  |
| standard deviation                              | ± 9.3  | -  |  |
| Weight<br>Units: kg                             |        |    |  |
| arithmetic mean                                 | 76.5   |    |  |
| standard deviation                              | ± 12.0 | -  |  |
| BMI<br>Units: kg/m2                             |        |    |  |
| arithmetic mean                                 | 27.4   |    |  |
| standard deviation                              | ± 4.6  | -  |  |
| Temperature<br>Units: celsius temperature       |        |    |  |
| arithmetic mean                                 | 36.0   |    |  |
| standard deviation                              | ± 0.4  | -  |  |
| Respiratory rate<br>Units: breaths per minute   |        |    |  |
| arithmetic mean                                 | 16.1   |    |  |
| standard deviation                              | ± 2.1  | -  |  |
| Systolic blood pressure<br>Units: mmHg          |        |    |  |
| arithmetic mean                                 | 130.1  |    |  |



|                                                                                              |                   |   |  |
|----------------------------------------------------------------------------------------------|-------------------|---|--|
| standard deviation                                                                           | ± 22.6            | - |  |
| Diastolic blood pressure<br>Units: mmHg<br>arithmetic mean<br>standard deviation             | 75.7<br>± 12.9    | - |  |
| Pulse<br>Units: lpm<br>arithmetic mean<br>standard deviation                                 | 72.5<br>± 10.7    | - |  |
| BCR-ABL molecular response<br>Units: not applicable<br>arithmetic mean<br>standard deviation | 0.0016<br>± 0.00  | - |  |
| Sokal risk<br>Units: NA<br>arithmetic mean<br>standard deviation                             | 0.58<br>± 0.3     | - |  |
| Hasford score<br>Units: NA<br>arithmetic mean<br>standard deviation                          | 360.91<br>± 351.6 | - |  |
| Eutos score<br>Units: NA<br>arithmetic mean<br>standard deviation                            | 14.33<br>± 17.4   | - |  |
| PR interval<br>Units: ms<br>arithmetic mean<br>standard deviation                            | 144.6<br>± 17.3   | - |  |
| QRS complex<br>Units: ms<br>arithmetic mean<br>standard deviation                            | 98.9<br>± 16.8    | - |  |
| QTcF interval<br>Units: ms<br>arithmetic mean<br>standard deviation                          | 393.6<br>± 63.4   | - |  |
| Heart rate<br>Units: bpm<br>arithmetic mean<br>standard deviation                            | 69.0<br>± 11.8    | - |  |
| RBC<br>Units: x106/uL<br>arithmetic mean<br>standard deviation                               | 4.2<br>± 0.5      | - |  |
| Hemoglobin<br>Units: g/dL<br>arithmetic mean<br>standard deviation                           | 13.8<br>± 1.3     | - |  |
| Hematocrit<br>Units: percentage<br>arithmetic mean                                           | 40.1              |   |  |

|                            |        |   |  |
|----------------------------|--------|---|--|
| standard deviation         | ± 4.1  | - |  |
| Platelets                  |        |   |  |
| Units: x10 <sup>9</sup>    |        |   |  |
| arithmetic mean            | 235.5  |   |  |
| standard deviation         | ± 43.0 | - |  |
| Leucocytes                 |        |   |  |
| Units: x10 <sup>9</sup>    |        |   |  |
| arithmetic mean            | 5.6    |   |  |
| standard deviation         | ± 1.6  | - |  |
| VCM                        |        |   |  |
| Units: f/L                 |        |   |  |
| arithmetic mean            | 95.0   |   |  |
| standard deviation         | ± 4.0  | - |  |
| Neutrophils absolute count |        |   |  |
| Units: 10 <sup>9</sup> /L  |        |   |  |
| arithmetic mean            | 3.1    |   |  |
| standard deviation         | ± 1.1  | - |  |
| Neutrophils                |        |   |  |
| Units: percentage          |        |   |  |
| arithmetic mean            | 55.2   |   |  |
| standard deviation         | ± 8.7  | - |  |
| Lymphocytes                |        |   |  |
| Units: percentage          |        |   |  |
| arithmetic mean            | 32.4   |   |  |
| standard deviation         | ± 7.5  | - |  |
| Monocytes                  |        |   |  |
| Units: percentage          |        |   |  |
| arithmetic mean            | 8.1    |   |  |
| standard deviation         | ± 1.9  | - |  |
| Eosinophils                |        |   |  |
| Units: percentage          |        |   |  |
| arithmetic mean            | 3.4    |   |  |
| standard deviation         | ± 2.4  | - |  |
| Basophils                  |        |   |  |
| Units: percentage          |        |   |  |
| arithmetic mean            | 0.8    |   |  |
| standard deviation         | ± 0.4  | - |  |
| WBC                        |        |   |  |
| Units: NA                  |        |   |  |
| arithmetic mean            | 100.0  |   |  |
| standard deviation         | ± 0.2  | - |  |
| Glucose                    |        |   |  |
| Units: mg/dL               |        |   |  |
| arithmetic mean            | 100.9  |   |  |
| standard deviation         | ± 9.9  | - |  |
| BUN                        |        |   |  |
| Units: mg/dL               |        |   |  |
| arithmetic mean            | 32.4   |   |  |
| standard deviation         | ± 7.3  | - |  |
| Creatinine                 |        |   |  |
| Units: mg/dL               |        |   |  |
| arithmetic mean            | 1.0    |   |  |

|                      |         |   |  |
|----------------------|---------|---|--|
| standard deviation   | ± 0.2   | - |  |
| Albumin              |         |   |  |
| Units: g/dL          |         |   |  |
| arithmetic mean      | 5.9     |   |  |
| standard deviation   | ± 7.1   | - |  |
| AST                  |         |   |  |
| Units: U/L           |         |   |  |
| arithmetic mean      | 21.9    |   |  |
| standard deviation   | ± 4.1   | - |  |
| ALT                  |         |   |  |
| Units: U/L           |         |   |  |
| arithmetic mean      | 20.4    |   |  |
| standard deviation   | ± 8.4   | - |  |
| Alkaline phosphatase |         |   |  |
| Units: UI/L          |         |   |  |
| arithmetic mean      | 68.8    |   |  |
| standard deviation   | ± 21.2  | - |  |
| Total bilirubin      |         |   |  |
| Units: mg/dL         |         |   |  |
| arithmetic mean      | 0.5     |   |  |
| standard deviation   | ± 0.2   | - |  |
| Indirect bilirubin   |         |   |  |
| Units: mg/dL         |         |   |  |
| arithmetic mean      | 0.5     |   |  |
| standard deviation   | ± 0.2   | - |  |
| Direct bilirubin     |         |   |  |
| Units: mg/dL         |         |   |  |
| arithmetic mean      | 0.2     |   |  |
| standard deviation   | ± 0.1   | - |  |
| Troponin             |         |   |  |
| Units: ng/mL         |         |   |  |
| arithmetic mean      | 9.4     |   |  |
| standard deviation   | ± 5.9   | - |  |
| Troponin T           |         |   |  |
| Units: ng/mL         |         |   |  |
| arithmetic mean      | 10.3    |   |  |
| standard deviation   | ± 4.8   | - |  |
| NT-proBNP            |         |   |  |
| Units: pg/mL         |         |   |  |
| arithmetic mean      | 51.5    |   |  |
| standard deviation   | ± 57.5  | - |  |
| BNP                  |         |   |  |
| Units: pg/mL         |         |   |  |
| arithmetic mean      | 113.8   |   |  |
| standard deviation   | ± 106.9 | - |  |
| Phosphorus           |         |   |  |
| Units: mg/dL         |         |   |  |
| arithmetic mean      | 2.7     |   |  |
| standard deviation   | ± 0.5   | - |  |
| Magnesium            |         |   |  |
| Units: mg/dL         |         |   |  |
| arithmetic mean      | 2.0     |   |  |

|                    |        |   |  |
|--------------------|--------|---|--|
| standard deviation | ± 0.1  | - |  |
| Sodium             |        |   |  |
| Units: mmol/L      |        |   |  |
| arithmetic mean    | 140.9  |   |  |
| standard deviation | ± 2.0  | - |  |
| Potassium          |        |   |  |
| Units: mmol/L      |        |   |  |
| arithmetic mean    | 4.2    |   |  |
| standard deviation | ± 0.3  | - |  |
| Calcium            |        |   |  |
| Units: mg/dL       |        |   |  |
| arithmetic mean    | 9.2    |   |  |
| standard deviation | ± 0.4  | - |  |
| Amilase            |        |   |  |
| Units: U/L         |        |   |  |
| arithmetic mean    | 68.4   |   |  |
| standard deviation | ± 25.2 | - |  |
| GGT                |        |   |  |
| Units: U/L         |        |   |  |
| arithmetic mean    | 20.6   |   |  |
| standard deviation | ± 14.0 | - |  |
| LDH                |        |   |  |
| Units: U/L         |        |   |  |
| arithmetic mean    | 213.3  |   |  |
| standard deviation | ± 46.3 | - |  |
| Lipase             |        |   |  |
| Units: U/L         |        |   |  |
| arithmetic mean    | 82.6   |   |  |
| standard deviation | ± 72.1 | - |  |
| Total cholesterol  |        |   |  |
| Units: mg/dL       |        |   |  |
| arithmetic mean    | 175.7  |   |  |
| standard deviation | ± 30.7 | - |  |
| Triglycerides      |        |   |  |
| Units: mg/dL       |        |   |  |
| arithmetic mean    | 113.7  |   |  |
| standard deviation | ± 58.6 | - |  |
| HbA1c              |        |   |  |
| Units: percentage  |        |   |  |
| arithmetic mean    | 5.3    |   |  |
| standard deviation | ± 0.3  | - |  |
| C-reactive protein |        |   |  |
| Units: mg/dL       |        |   |  |
| arithmetic mean    | 0.3    |   |  |
| standard deviation | ± 0.3  | - |  |

### Subject analysis sets

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | TFR Phase Group |
| Subject analysis set type  | Full analysis   |

Subject analysis set description:

Number of patients who entered ponatinib TFR phase

|                                                                                                      |                            |
|------------------------------------------------------------------------------------------------------|----------------------------|
| Subject analysis set title                                                                           | Consolidation Phase Group  |
| Subject analysis set type                                                                            | Full analysis              |
| Subject analysis set description:                                                                    |                            |
| Patients who entered the Ponatinib consolidation phase                                               |                            |
| Subject analysis set title                                                                           | Safety analysis set        |
| Subject analysis set type                                                                            | Safety analysis            |
| Subject analysis set description:                                                                    |                            |
| All patients who received at least one dose of ponatinib                                             |                            |
| Subject analysis set title                                                                           | Patients who restarted TKI |
| Subject analysis set type                                                                            | Full analysis              |
| Subject analysis set description:                                                                    |                            |
| Patients who lost molecular response and restart imatinib or any Tyrosine Kinase-Inhibitor treatment |                            |

| Reporting group values                             | TFR Phase Group | Consolidation Phase Group | Safety analysis set |
|----------------------------------------------------|-----------------|---------------------------|---------------------|
| Number of subjects                                 | 19              | 23                        | 23                  |
| Age categorical                                    |                 |                           |                     |
| Units: Subjects                                    |                 |                           |                     |
| In utero                                           | 0               | 0                         | 0                   |
| Preterm newborn infants (gestational age < 37 wks) | 0               | 0                         | 0                   |
| Newborns (0-27 days)                               | 0               | 0                         | 0                   |
| Infants and toddlers (28 days-23 months)           | 0               | 0                         | 0                   |
| Children (2-11 years)                              | 0               | 0                         | 0                   |
| Adolescents (12-17 years)                          | 0               | 0                         | 0                   |
| Adults (18-64 years)                               | 18              | 19                        | 19                  |
| From 65-84 years                                   | 1               | 4                         | 4                   |
| 85 years and over                                  | 0               | 0                         | 0                   |
| Age continuous                                     |                 |                           |                     |
| Units: years                                       |                 |                           |                     |
| arithmetic mean                                    |                 |                           |                     |
| standard deviation                                 | ±               | ±                         | ±                   |
| Gender categorical                                 |                 |                           |                     |
| Units: Subjects                                    |                 |                           |                     |
| Female                                             |                 |                           |                     |
| Male                                               |                 |                           |                     |
| Race                                               |                 |                           |                     |
| Units: Subjects                                    |                 |                           |                     |
| Caucasian                                          |                 |                           |                     |
| Latin                                              |                 |                           |                     |
| ECOG                                               |                 |                           |                     |
| Units: Subjects                                    |                 |                           |                     |
| 0-zero                                             |                 |                           |                     |
| 1-one                                              |                 |                           |                     |
| Physical examination - General                     |                 |                           |                     |
| Units: Subjects                                    |                 |                           |                     |
| Normal                                             |                 |                           |                     |
| Abnormal                                           |                 |                           |                     |
| Physical examination - Skin                        |                 |                           |                     |
| Units: Subjects                                    |                 |                           |                     |
| Normal                                             |                 |                           |                     |
| Abnormal                                           |                 |                           |                     |

|                                                       |  |  |  |
|-------------------------------------------------------|--|--|--|
| Physical examination - Neck<br>Units: Subjects        |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Ears<br>Units: Subjects        |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Eyes<br>Units: Subjects        |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Nose<br>Units: Subjects        |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Heart<br>Units: Subjects       |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Throat<br>Units: Subjects      |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Lungs<br>Units: Subjects       |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Abdomen<br>Units: Subjects     |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Back<br>Units: Subjects        |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Lymph nodes<br>Units: Subjects |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Neurologic<br>Units: Subjects  |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Extremities<br>Units: Subjects |  |  |  |
| Normal                                                |  |  |  |
| Abnormal                                              |  |  |  |
| Physical examination - Vascular<br>Units: Subjects    |  |  |  |
| Normal                                                |  |  |  |

|                                                                                    |   |   |   |
|------------------------------------------------------------------------------------|---|---|---|
| Abnormal                                                                           |   |   |   |
| Physical examination - Extramedular<br>Units: Subjects                             |   |   |   |
| Normal<br>Abnormal                                                                 |   |   |   |
| Electrocardiogram<br>Units: Subjects                                               |   |   |   |
| Normal<br>Abnormal                                                                 |   |   |   |
| Echocardiogram<br>Units: Subjects                                                  |   |   |   |
| Normal<br>Abnormal                                                                 |   |   |   |
| Pregnancy test<br>Units: Subjects                                                  |   |   |   |
| Negative<br>Not applicable                                                         |   |   |   |
| Hepatitis B surface antibody<br>Units: Subjects                                    |   |   |   |
| Negative<br>Positive<br>No data                                                    |   |   |   |
| Hepatitis B surface antigen<br>Units: Subjects                                     |   |   |   |
| Negative<br>Positive<br>No data                                                    |   |   |   |
| Hepatitis B core<br>Units: Subjects                                                |   |   |   |
| Negative<br>Positive<br>No data                                                    |   |   |   |
| Height<br>Units: cm<br>arithmetic mean<br>standard deviation                       | ± | ± | ± |
| Weight<br>Units: kg<br>arithmetic mean<br>standard deviation                       | ± | ± | ± |
| BMI<br>Units: kg/m2<br>arithmetic mean<br>standard deviation                       | ± | ± | ± |
| Temperature<br>Units: celsius temperature<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Respiratory rate<br>Units: breaths per minute<br>arithmetic mean                   |   |   |   |

|                                                                                              |   |   |   |
|----------------------------------------------------------------------------------------------|---|---|---|
| standard deviation                                                                           | ± | ± | ± |
| Systolic blood pressure<br>Units: mmHg<br>arithmetic mean<br>standard deviation              | ± | ± | ± |
| Diastolic blood pressure<br>Units: mmHg<br>arithmetic mean<br>standard deviation             | ± | ± | ± |
| Pulse<br>Units: lpm<br>arithmetic mean<br>standard deviation                                 | ± | ± | ± |
| BCR-ABL molecular response<br>Units: not applicable<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sokal risk<br>Units: NA<br>arithmetic mean<br>standard deviation                             | ± | ± | ± |
| Hasford score<br>Units: NA<br>arithmetic mean<br>standard deviation                          | ± | ± | ± |
| Eutos score<br>Units: NA<br>arithmetic mean<br>standard deviation                            | ± | ± | ± |
| PR interval<br>Units: ms<br>arithmetic mean<br>standard deviation                            | ± | ± | ± |
| QRS complex<br>Units: ms<br>arithmetic mean<br>standard deviation                            | ± | ± | ± |
| QTcF interval<br>Units: ms<br>arithmetic mean<br>standard deviation                          | ± | ± | ± |
| Heart rate<br>Units: bpm<br>arithmetic mean<br>standard deviation                            | ± | ± | ± |
| RBC<br>Units: x106/uL<br>arithmetic mean<br>standard deviation                               | ± | ± | ± |
| Hemoglobin<br>Units: g/dL<br>arithmetic mean                                                 |   |   |   |



|                            |   |   |   |
|----------------------------|---|---|---|
| standard deviation         | ± | ± | ± |
| Hematocrit                 |   |   |   |
| Units: percentage          |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Platelets                  |   |   |   |
| Units: x10 <sup>9</sup>    |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Leucocytes                 |   |   |   |
| Units: x10 <sup>9</sup>    |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| VCM                        |   |   |   |
| Units: f/L                 |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Neutrophils absolute count |   |   |   |
| Units: 10 <sup>9</sup> /L  |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Neutrophils                |   |   |   |
| Units: percentage          |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Lymphocytes                |   |   |   |
| Units: percentage          |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Monocytes                  |   |   |   |
| Units: percentage          |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Eosinophils                |   |   |   |
| Units: percentage          |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Basophils                  |   |   |   |
| Units: percentage          |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| WBC                        |   |   |   |
| Units: NA                  |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| Glucose                    |   |   |   |
| Units: mg/dL               |   |   |   |
| arithmetic mean            |   |   |   |
| standard deviation         | ± | ± | ± |
| BUN                        |   |   |   |
| Units: mg/dL               |   |   |   |
| arithmetic mean            |   |   |   |

|                                                                              |   |   |   |
|------------------------------------------------------------------------------|---|---|---|
| standard deviation                                                           | ± | ± | ± |
| Creatinine<br>Units: mg/dL<br>arithmetic mean<br>standard deviation          | ± | ± | ± |
| Albumin<br>Units: g/dL<br>arithmetic mean<br>standard deviation              | ± | ± | ± |
| AST<br>Units: U/L<br>arithmetic mean<br>standard deviation                   | ± | ± | ± |
| ALT<br>Units: U/L<br>arithmetic mean<br>standard deviation                   | ± | ± | ± |
| Alkaline phosphatase<br>Units: UI/L<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Total bilirubin<br>Units: mg/dL<br>arithmetic mean<br>standard deviation     | ± | ± | ± |
| Indirect bilirubin<br>Units: mg/dL<br>arithmetic mean<br>standard deviation  | ± | ± | ± |
| Direct bilirubin<br>Units: mg/dL<br>arithmetic mean<br>standard deviation    | ± | ± | ± |
| Troponin<br>Units: ng/mL<br>arithmetic mean<br>standard deviation            | ± | ± | ± |
| Troponin T<br>Units: ng/mL<br>arithmetic mean<br>standard deviation          | ± | ± | ± |
| NT-proBNP<br>Units: pg/mL<br>arithmetic mean<br>standard deviation           | ± | ± | ± |
| BNP<br>Units: pg/mL<br>arithmetic mean<br>standard deviation                 | ± | ± | ± |
| Phosphorus<br>Units: mg/dL<br>arithmetic mean                                |   |   |   |

|                               |                            |   |   |
|-------------------------------|----------------------------|---|---|
| standard deviation            | ±                          | ± | ± |
| Magnesium                     |                            |   |   |
| Units: mg/dL                  |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Sodium                        |                            |   |   |
| Units: mmol/L                 |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Potassium                     |                            |   |   |
| Units: mmol/L                 |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Calcium                       |                            |   |   |
| Units: mg/dL                  |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Amilase                       |                            |   |   |
| Units: U/L                    |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| GGT                           |                            |   |   |
| Units: U/L                    |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| LDH                           |                            |   |   |
| Units: U/L                    |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Lipase                        |                            |   |   |
| Units: U/L                    |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Total cholesterol             |                            |   |   |
| Units: mg/dL                  |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| Triglycerides                 |                            |   |   |
| Units: mg/dL                  |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| HbA1c                         |                            |   |   |
| Units: percentage             |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| C-reactive protein            |                            |   |   |
| Units: mg/dL                  |                            |   |   |
| arithmetic mean               |                            |   |   |
| standard deviation            | ±                          | ± | ± |
| <b>Reporting group values</b> | Patients who restarted TKI |   |   |

|                                                       |   |  |  |
|-------------------------------------------------------|---|--|--|
| Number of subjects                                    | 5 |  |  |
| Age categorical                                       |   |  |  |
| Units: Subjects                                       |   |  |  |
| In utero                                              | 0 |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0 |  |  |
| Newborns (0-27 days)                                  | 0 |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0 |  |  |
| Children (2-11 years)                                 | 0 |  |  |
| Adolescents (12-17 years)                             | 0 |  |  |
| Adults (18-64 years)                                  | 5 |  |  |
| From 65-84 years                                      | 0 |  |  |
| 85 years and over                                     | 0 |  |  |
| Age continuous                                        |   |  |  |
| Units: years                                          |   |  |  |
| arithmetic mean                                       |   |  |  |
| standard deviation                                    | ± |  |  |
| Gender categorical                                    |   |  |  |
| Units: Subjects                                       |   |  |  |
| Female                                                |   |  |  |
| Male                                                  |   |  |  |
| Race                                                  |   |  |  |
| Units: Subjects                                       |   |  |  |
| Caucasian                                             |   |  |  |
| Latin                                                 |   |  |  |
| ECOG                                                  |   |  |  |
| Units: Subjects                                       |   |  |  |
| 0-zero                                                |   |  |  |
| 1-one                                                 |   |  |  |
| Physical examination - General                        |   |  |  |
| Units: Subjects                                       |   |  |  |
| Normal                                                |   |  |  |
| Abnormal                                              |   |  |  |
| Physical examination - Skin                           |   |  |  |
| Units: Subjects                                       |   |  |  |
| Normal                                                |   |  |  |
| Abnormal                                              |   |  |  |
| Physical examination - Neck                           |   |  |  |
| Units: Subjects                                       |   |  |  |
| Normal                                                |   |  |  |
| Abnormal                                              |   |  |  |
| Physical examination - Ears                           |   |  |  |
| Units: Subjects                                       |   |  |  |
| Normal                                                |   |  |  |
| Abnormal                                              |   |  |  |
| Physical examination - Eyes                           |   |  |  |
| Units: Subjects                                       |   |  |  |
| Normal                                                |   |  |  |
| Abnormal                                              |   |  |  |
| Physical examination - Nose                           |   |  |  |
| Units: Subjects                                       |   |  |  |

|                                                        |  |  |  |
|--------------------------------------------------------|--|--|--|
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Heart<br>Units: Subjects        |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Throat<br>Units: Subjects       |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Lungs<br>Units: Subjects        |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Abdomen<br>Units: Subjects      |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Back<br>Units: Subjects         |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Lymph nodes<br>Units: Subjects  |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Neurologic<br>Units: Subjects   |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Extremities<br>Units: Subjects  |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Vascular<br>Units: Subjects     |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Physical examination - Extramedular<br>Units: Subjects |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Electrocardiogram<br>Units: Subjects                   |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Echocardiogram<br>Units: Subjects                      |  |  |  |
| Normal<br>Abnormal                                     |  |  |  |
| Pregnancy test                                         |  |  |  |

|                              |   |  |  |
|------------------------------|---|--|--|
| Units: Subjects              |   |  |  |
| Negative                     |   |  |  |
| Not applicable               |   |  |  |
| Hepatitis B surface antibody |   |  |  |
| Units: Subjects              |   |  |  |
| Negative                     |   |  |  |
| Positive                     |   |  |  |
| No data                      |   |  |  |
| Hepatitis B surface antigen  |   |  |  |
| Units: Subjects              |   |  |  |
| Negative                     |   |  |  |
| Positive                     |   |  |  |
| No data                      |   |  |  |
| Hepatitis B core             |   |  |  |
| Units: Subjects              |   |  |  |
| Negative                     |   |  |  |
| Positive                     |   |  |  |
| No data                      |   |  |  |
| Height                       |   |  |  |
| Units: cm                    |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| Weight                       |   |  |  |
| Units: kg                    |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| BMI                          |   |  |  |
| Units: kg/m2                 |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| Temperature                  |   |  |  |
| Units: celsius temperature   |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| Respiratory rate             |   |  |  |
| Units: breaths per minute    |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| Systolic blood pressure      |   |  |  |
| Units: mmHg                  |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| Diastolic blood pressure     |   |  |  |
| Units: mmHg                  |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| Pulse                        |   |  |  |
| Units: lpm                   |   |  |  |
| arithmetic mean              |   |  |  |
| standard deviation           | ± |  |  |
| BCR-ABL molecular response   |   |  |  |

|                                                                          |       |  |  |
|--------------------------------------------------------------------------|-------|--|--|
| Units: not applicable<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| Sokal risk<br>Units: NA<br>arithmetic mean<br>standard deviation         | $\pm$ |  |  |
| Hasford score<br>Units: NA<br>arithmetic mean<br>standard deviation      | $\pm$ |  |  |
| Eutos score<br>Units: NA<br>arithmetic mean<br>standard deviation        | $\pm$ |  |  |
| PR interval<br>Units: ms<br>arithmetic mean<br>standard deviation        | $\pm$ |  |  |
| QRS complex<br>Units: ms<br>arithmetic mean<br>standard deviation        | $\pm$ |  |  |
| QTcF interval<br>Units: ms<br>arithmetic mean<br>standard deviation      | $\pm$ |  |  |
| Heart rate<br>Units: bpm<br>arithmetic mean<br>standard deviation        | $\pm$ |  |  |
| RBC<br>Units: x106/uL<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| Hemoglobin<br>Units: g/dL<br>arithmetic mean<br>standard deviation       | $\pm$ |  |  |
| Hematocrit<br>Units: percentage<br>arithmetic mean<br>standard deviation | $\pm$ |  |  |
| Platelets<br>Units: x109<br>arithmetic mean<br>standard deviation        | $\pm$ |  |  |
| Leucocytes<br>Units: x109<br>arithmetic mean<br>standard deviation       | $\pm$ |  |  |
| VCM                                                                      |       |  |  |

|                                                                                     |       |  |  |
|-------------------------------------------------------------------------------------|-------|--|--|
| Units: f/L<br>arithmetic mean<br>standard deviation                                 | $\pm$ |  |  |
| Neutrophils absolute count<br>Units: 109/L<br>arithmetic mean<br>standard deviation | $\pm$ |  |  |
| Neutrophils<br>Units: percentage<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| Lymphocytes<br>Units: percentage<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| Monocytes<br>Units: percentage<br>arithmetic mean<br>standard deviation             | $\pm$ |  |  |
| Eosinophils<br>Units: percentage<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| Basophils<br>Units: percentage<br>arithmetic mean<br>standard deviation             | $\pm$ |  |  |
| WBC<br>Units: NA<br>arithmetic mean<br>standard deviation                           | $\pm$ |  |  |
| Glucose<br>Units: mg/dL<br>arithmetic mean<br>standard deviation                    | $\pm$ |  |  |
| BUN<br>Units: mg/dL<br>arithmetic mean<br>standard deviation                        | $\pm$ |  |  |
| Creatinine<br>Units: mg/dL<br>arithmetic mean<br>standard deviation                 | $\pm$ |  |  |
| Albumin<br>Units: g/dL<br>arithmetic mean<br>standard deviation                     | $\pm$ |  |  |
| AST<br>Units: U/L<br>arithmetic mean<br>standard deviation                          | $\pm$ |  |  |
| ALT                                                                                 |       |  |  |



|                                                                              |       |  |  |
|------------------------------------------------------------------------------|-------|--|--|
| Units: U/L<br>arithmetic mean<br>standard deviation                          | $\pm$ |  |  |
| Alkaline phosphatase<br>Units: UI/L<br>arithmetic mean<br>standard deviation | $\pm$ |  |  |
| Total bilirubin<br>Units: mg/dL<br>arithmetic mean<br>standard deviation     | $\pm$ |  |  |
| Indirect bilirubin<br>Units: mg/dL<br>arithmetic mean<br>standard deviation  | $\pm$ |  |  |
| Direct bilirubin<br>Units: mg/dL<br>arithmetic mean<br>standard deviation    | $\pm$ |  |  |
| Troponin<br>Units: ng/mL<br>arithmetic mean<br>standard deviation            | $\pm$ |  |  |
| Troponin T<br>Units: ng/mL<br>arithmetic mean<br>standard deviation          | $\pm$ |  |  |
| NT-proBNP<br>Units: pg/mL<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| BNP<br>Units: pg/mL<br>arithmetic mean<br>standard deviation                 | $\pm$ |  |  |
| Phosphorus<br>Units: mg/dL<br>arithmetic mean<br>standard deviation          | $\pm$ |  |  |
| Magnesium<br>Units: mg/dL<br>arithmetic mean<br>standard deviation           | $\pm$ |  |  |
| Sodium<br>Units: mmol/L<br>arithmetic mean<br>standard deviation             | $\pm$ |  |  |
| Potassium<br>Units: mmol/L<br>arithmetic mean<br>standard deviation          | $\pm$ |  |  |
| Calcium                                                                      |       |  |  |

|                                                                             |       |  |  |
|-----------------------------------------------------------------------------|-------|--|--|
| Units: mg/dL<br>arithmetic mean<br>standard deviation                       | $\pm$ |  |  |
| Amilase<br>Units: U/L<br>arithmetic mean<br>standard deviation              | $\pm$ |  |  |
| GGT<br>Units: U/L<br>arithmetic mean<br>standard deviation                  | $\pm$ |  |  |
| LDH<br>Units: U/L<br>arithmetic mean<br>standard deviation                  | $\pm$ |  |  |
| Lipase<br>Units: U/L<br>arithmetic mean<br>standard deviation               | $\pm$ |  |  |
| Total cholesterol<br>Units: mg/dL<br>arithmetic mean<br>standard deviation  | $\pm$ |  |  |
| Triglycerides<br>Units: mg/dL<br>arithmetic mean<br>standard deviation      | $\pm$ |  |  |
| HbA1c<br>Units: percentage<br>arithmetic mean<br>standard deviation         | $\pm$ |  |  |
| C-reactive protein<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | $\pm$ |  |  |

## End points

### End points reporting groups

|                                                                                                                                           |                            |
|-------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Reporting group title                                                                                                                     | Single-arm                 |
| Reporting group description:<br>Patients that received ponatinib 15 mg during the consolidation phase                                     |                            |
| Reporting group title                                                                                                                     | Single-arm                 |
| Reporting group description: -                                                                                                            |                            |
| Subject analysis set title                                                                                                                | TFR Phase Group            |
| Subject analysis set type                                                                                                                 | Full analysis              |
| Subject analysis set description:<br>Number of patients who entered ponatinib TFR phase                                                   |                            |
| Subject analysis set title                                                                                                                | Consolidation Phase Group  |
| Subject analysis set type                                                                                                                 | Full analysis              |
| Subject analysis set description:<br>Patients who entered the Ponatinib consolidation phase                                               |                            |
| Subject analysis set title                                                                                                                | Safety analysis set        |
| Subject analysis set type                                                                                                                 | Safety analysis            |
| Subject analysis set description:<br>All patients who received at least one dose of ponatinib                                             |                            |
| Subject analysis set title                                                                                                                | Patients who restarted TKI |
| Subject analysis set type                                                                                                                 | Full analysis              |
| Subject analysis set description:<br>Patients who lost molecular response and restart imatinib or any Tyrosine Kinase-Inhibitor treatment |                            |

### Primary: Proportion of patients without confirmed loss of MR4 or MMR within 48 weeks after ponatinib TFR

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Proportion of patients without confirmed loss of MR4 or MMR within 48 weeks after ponatinib TFR |
| End point description:<br>The primary efficacy variable was the binary outcome measure, the proportion of patients without confirmed loss of MR4 or loss of MMR within 48 weeks of ponatinib TFR. This variable was defined as the number of patients with no documented confirmed loss of MR4 or no loss of MMR and no restart of imatinib therapy in the first 48 weeks after the start of the ponatinib TFR phase divided by the number of patients who entered the ponatinib TFR phase (full analysis set). |                                                                                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Primary                                                                                         |
| End point timeframe:<br>From ponatinib discontinuation until 48 weeks of follow-up in TFR phase.                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                 |

| End point values                   | Single-arm      | TFR Phase Group      |  |  |
|------------------------------------|-----------------|----------------------|--|--|
| Subject group type                 | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed        | 19              | 19                   |  |  |
| Units: Proportion                  |                 |                      |  |  |
| Without loss of molecular response | 13              | 13                   |  |  |
| Loss of molecular response         | 6               | 6                    |  |  |

## Statistical analyses

|                                                                                                      |                              |
|------------------------------------------------------------------------------------------------------|------------------------------|
| <b>Statistical analysis title</b>                                                                    | Primary endpoint analysis    |
| Statistical analysis description:                                                                    |                              |
| Primary Endpoint Analysis: Proportion of Patients Maintaining MR4/MMR at 48 Weeks Post-Ponatinib TFR |                              |
| Comparison groups                                                                                    | Single-arm v TFR Phase Group |
| Number of subjects included in analysis                                                              | 38                           |
| Analysis specification                                                                               | Pre-specified                |
| Analysis type                                                                                        | other <sup>[1]</sup>         |
| P-value                                                                                              | < 0.05 <sup>[2]</sup>        |
| Method                                                                                               | Clopper-Pearson exact CI     |
| Parameter estimate                                                                                   | Clopper-Pearson exact CI     |
| Point estimate                                                                                       | 0.684                        |
| Confidence interval                                                                                  |                              |
| level                                                                                                | 95 %                         |
| sides                                                                                                | 2-sided                      |
| lower limit                                                                                          | 0.434                        |
| upper limit                                                                                          | 0.874                        |

Notes:

[1] - Single-arm proportion analysis with Clopper-Pearson CI. IMPORTANT NOTE: This analysis was performed in the group of the patients who entered the TFR phase only (n=19).

[2] - Exact Clopper-Pearson confidence interval was used to assess the proportion of patients maintaining MR4/MMR at 48 weeks in TFR phase. The null hypothesis was rejected if the lower limit of the 95% confidence interval was greater than 0.10 (10%).

## Secondary: Proportion of patients without documented loss of MR4 or loss of MMR at 72 and 96 weeks after ponatinib discontinuation

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of patients without documented loss of MR4 or loss of MMR at 72 and 96 weeks after ponatinib discontinuation |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Proportion of patients without documented loss of MR4 or loss of MMR at 72 and 96 weeks after discontinuation of ponatinib treatment. This proportion of patients was calculated by dividing the number of patients with no documented confirmed loss of MR4 or loss of MMR and no reinitiation of imatinib at 72 or 96 weeks after discontinuation of ponatinib by the number of patients who entered the ponatinib TFR phase (full analysis set).

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

End point timeframe:

From ponatinib discontinuation until 72 and 96 weeks of follow-up in TFR phase.

| End point values                   | Single-arm        | TFR Phase Group      |  |  |
|------------------------------------|-------------------|----------------------|--|--|
| Subject group type                 | Reporting group   | Subject analysis set |  |  |
| Number of subjects analysed        | 19 <sup>[3]</sup> | 19                   |  |  |
| Units: Proportion                  |                   |                      |  |  |
| Without loss of molecular response | 13                | 13                   |  |  |
| Loss molecular response            | 6                 | 6                    |  |  |

Notes:

[3] - The number of patients who entered the TFR phase is 19.

## Statistical analyses

|                                                                                               |                                    |
|-----------------------------------------------------------------------------------------------|------------------------------------|
| <b>Statistical analysis title</b>                                                             | Analysis of TFR at 72 and 76 weeks |
| Statistical analysis description:                                                             |                                    |
| Analysis of Treatment-Free Remission (TFR) at 72 and 96 Weeks (visit 24 and 25, respectively) |                                    |
| Comparison groups                                                                             | Single-arm v TFR Phase Group       |
| Number of subjects included in analysis                                                       | 38                                 |
| Analysis specification                                                                        | Pre-specified                      |
| Analysis type                                                                                 | other <sup>[4]</sup>               |
| P-value                                                                                       | < 0.05                             |
| Method                                                                                        | Clopper-Pearson exact CI           |
| Parameter estimate                                                                            | Clopper-Pearson exact CI           |
| Point estimate                                                                                | 0.68                               |
| Confidence interval                                                                           |                                    |
| level                                                                                         | 95 %                               |
| sides                                                                                         | 2-sided                            |
| lower limit                                                                                   | 0.43                               |
| upper limit                                                                                   | 0.87                               |

Notes:

[4] - Single-arm proportion analysis with Clopper-Pearson CI

### Secondary: Progression-Free Survival (PFS) after ponatinib discontinuation

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Progression-Free Survival (PFS) after ponatinib discontinuation |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                 |
| Progression free survival (PFS): Estimation of PFS after discontinuation of ponatinib was calculated using the Kaplan-Meier (KM) method. PFS was measured from the date of discontinuation of ponatinib therapy to the date of the earliest of the following events: progression to AP/BC or death from any cause. For patients who are not known to have progressed or died on or before the cut-off date for the KM analysis, the PFS interval is right censored to the date of the last assessment of molecular response status or the cut-off date, whichever is earlier. |                                                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                                       |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                 |
| From ponatinib discontinuation until progression to AP/BC, death, or last molecular response assessment before data cut-off                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                 |

| End point values            | TFR Phase Group      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 19                   |  |  |  |
| Units: Number of patients   | 19                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Treatment-Free Survival (TFS) after ponatinib discontinuation

|                        |                                                               |
|------------------------|---------------------------------------------------------------|
| End point title        | Treatment-Free Survival (TFS) after ponatinib discontinuation |
| End point description: |                                                               |

|                                                                                                                                              |           |
|----------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                                               | Secondary |
| End point timeframe:                                                                                                                         |           |
| From ponatinib discontinuation until loss of MMR, confirmed loss of MR4, restart of imatinib, progression to AP/BC, or death from any cause. |           |

| End point values            | Single-arm      | TFR Phase Group      |  |  |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type          | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed | 19              | 19                   |  |  |
| Units: Number of patients   | 15              | 15                   |  |  |

### Statistical analyses

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Statistical analysis title              | Kaplan-Meier Estimation of TFS |
| Comparison groups                       | Single-arm v TFR Phase Group   |
| Number of subjects included in analysis | 38                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[5]</sup>           |
| P-value                                 | < 0.05                         |
| Method                                  | Kaplan-Meier survival analysis |
| Parameter estimate                      | Kaplan-Meier survival analysis |
| Point estimate                          | 68.4                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 50.4                           |
| upper limit                             | 92.9                           |

Notes:

[5] - Kaplan-Meier survival analysis

### Secondary: Overall Survival (OS) after ponatinib discontinuation

|                                                                                                                                                                                                                                                                                                                                                                        |                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                        | Overall Survival (OS) after ponatinib discontinuation |
| End point description:                                                                                                                                                                                                                                                                                                                                                 |                                                       |
| Overall survival (OS): OS was defined as the time from the date of discontinuation of ponatinib therapy to the date of death from any cause. If a patient was not known to have died, OS was censored at the date of last contact (Figure 2). A similar method of analysis was used to estimate the time to regain MR4 from the date of restart of imatinib treatment. |                                                       |
| End point type                                                                                                                                                                                                                                                                                                                                                         | Secondary                                             |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                   |                                                       |
| From ponatinib discontinuation until death from any cause or last patient contact (censored)                                                                                                                                                                                                                                                                           |                                                       |

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| <b>End point values</b>     | TFR Phase Group      |  |  |  |
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 19                   |  |  |  |
| Units: Number of patients   | 19                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of patients who regained MR4 within 48 weeks after imatinib re-initiation

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Proportion of patients who regained MR4 within 48 weeks after imatinib re-initiation |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                      |
| The proportion of patients who regained MR4 within 48 weeks of imatinib treatment re- initiation following confirmed loss of MR4 or loss of MMR in the first 48 weeks subsequent to ponatinib cessation, was calculated by dividing the number of patients who re-achieve MR4 within 48 weeks of imatinib treatment re-initiation, following confirmed loss of MR4 or loss of MMR in the first 48 weeks subsequent to ponatinib cessation, by the number of patients who ceased ponatinib therapy and subsequently had confirmed loss of MR4 or lost MMR in the first 48 weeks following ponatinib cessation and re-initiated imatinib treatment. In the calculation of this proportion, patients who dropped out early without regaining MR4 during the re-treatment period were considered to be unsuccessful reinductions of MR4 and were counted in the denominator in the calculation of the rate. |                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Secondary                                                                            |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                      |
| From imatinib re-initiation until 48 weeks of follow-up                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                      |

|                               |                            |  |  |  |
|-------------------------------|----------------------------|--|--|--|
| <b>End point values</b>       | Patients who restarted TKI |  |  |  |
| Subject group type            | Subject analysis set       |  |  |  |
| Number of subjects analysed   | 5                          |  |  |  |
| Units: Proportion             |                            |  |  |  |
| Regain molecular response     | 4                          |  |  |  |
| Not regain molecular response | 1                          |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Plasma Concentration of Ponatinib Over Time

|                                                                                                 |                                             |
|-------------------------------------------------------------------------------------------------|---------------------------------------------|
| End point title                                                                                 | Plasma Concentration of Ponatinib Over Time |
| End point description:                                                                          |                                             |
| End point type                                                                                  | Other pre-specified                         |
| End point timeframe:                                                                            |                                             |
| From Day 0 of Ponatinib Consolidation Phase until TFR Visit 11 (Day 28 of Cycle 1 in TFR phase) |                                             |

|                                       |                              |  |  |  |
|---------------------------------------|------------------------------|--|--|--|
| <b>End point values</b>               | Consolidation<br>Phase Group |  |  |  |
| Subject group type                    | Subject analysis set         |  |  |  |
| Number of subjects analysed           | 17 <sup>[6]</sup>            |  |  |  |
| Units: ng/mL                          |                              |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 15.205 (10.030<br>to 20.431) |  |  |  |

Notes:

[6] - Number of patients at the visit 10 . Day 336 (end of treatment)

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first ponatinib dose until study completion, categorized by phase: Consolidation phase, TFR phase, and Imatinib restart phase

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Consolidation phase |
|-----------------------|---------------------|

Reporting group description:

AEs reported during the consolidation phase

|                       |           |
|-----------------------|-----------|
| Reporting group title | TFR phase |
|-----------------------|-----------|

Reporting group description:

AEs reported during TFR

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Imatinib restart |
|-----------------------|------------------|

Reporting group description:

AEs reported during imatinib restart period

| Serious adverse events                            | Consolidation phase | TFR phase      | Imatinib restart |
|---------------------------------------------------|---------------------|----------------|------------------|
| Total subjects affected by serious adverse events |                     |                |                  |
| subjects affected / exposed                       | 0 / 23 (0.00%)      | 0 / 19 (0.00%) | 0 / 5 (0.00%)    |
| number of deaths (all causes)                     | 0                   | 0              | 0                |
| number of deaths resulting from adverse events    | 0                   | 0              | 0                |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Consolidation phase | TFR phase         | Imatinib restart |
|-------------------------------------------------------|---------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events |                     |                   |                  |
| subjects affected / exposed                           | 23 / 23 (100.00%)   | 19 / 19 (100.00%) | 1 / 5 (20.00%)   |
| Vascular disorders                                    |                     |                   |                  |
| Essential hypertension                                |                     |                   |                  |
| subjects affected / exposed                           | 1 / 23 (4.35%)      | 0 / 19 (0.00%)    | 0 / 5 (0.00%)    |
| occurrences (all)                                     | 2                   | 0                 | 0                |
| Hypertension                                          |                     |                   |                  |
| subjects affected / exposed                           | 2 / 23 (8.70%)      | 1 / 19 (5.26%)    | 0 / 5 (0.00%)    |
| occurrences (all)                                     | 2                   | 2                 | 0                |
| Intermittent claudication                             |                     |                   |                  |

|                                                      |                 |                |                |
|------------------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Superficial thrombophlebitis                         |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Surgical and medical procedures                      |                 |                |                |
| Tooth extraction                                     |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 1 / 19 (5.26%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 1              | 0              |
| General disorders and administration site conditions |                 |                |                |
| Asthenia                                             |                 |                |                |
| subjects affected / exposed                          | 6 / 23 (26.09%) | 0 / 19 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)                                    | 8               | 0              | 2              |
| Chills                                               |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Decreased appetite                                   |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Feeling cold                                         |                 |                |                |
| subjects affected / exposed                          | 0 / 23 (0.00%)  | 1 / 19 (5.26%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 0               | 1              | 0              |
| Inflammation localized                               |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Influenza-like illness                               |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Malaise                                              |                 |                |                |
| subjects affected / exposed                          | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)                                    | 1               | 0              | 1              |
| Pyrexia                                              |                 |                |                |
| subjects affected / exposed                          | 2 / 23 (8.70%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                                    | 2               | 0              | 0              |
| Secretion discharge                                  |                 |                |                |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                            |                                                                                                                                                            |                                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                           | 1 / 23 (4.35%)<br>0                                                                                                                                        | 0 / 19 (0.00%)<br>0                                                                                                                                        | 0 / 5 (0.00%)<br>0                                                                                                         |
| Immune system disorders<br>Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                            | 0 / 23 (0.00%)<br>0                                                                                                                                        | 1 / 19 (5.26%)<br>1                                                                                                                                        | 0 / 5 (0.00%)<br>0                                                                                                         |
| Reproductive system and breast disorders<br>Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)<br><br>Nipple pain<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                | 2 / 23 (8.70%)<br>2<br><br>1 / 23 (4.35%)<br>1                                                                                                             | 0 / 19 (0.00%)<br>0<br><br>0 / 19 (0.00%)<br>0                                                                                                             | 0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0                                                                               |
| Respiratory, thoracic and mediastinal disorders<br>Asthma<br>subjects affected / exposed<br>occurrences (all)<br><br>Dysphonia<br>subjects affected / exposed<br>occurrences (all)<br><br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Pharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Tonsillitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Voice alteration<br>subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0<br><br>1 / 23 (4.35%)<br>1<br><br>1 / 23 (4.35%)<br>1<br><br>0 / 23 (0.00%)<br>0<br><br>0 / 23 (0.00%)<br>0<br><br>1 / 23 (4.35%)<br>1 | 1 / 19 (5.26%)<br>1<br><br>0 / 19 (0.00%)<br>0<br><br>0 / 19 (0.00%)<br>0<br><br>1 / 19 (5.26%)<br>1<br><br>1 / 19 (5.26%)<br>1<br><br>0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0 |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                      | 1 / 23 (4.35%)<br>1                                                                                                                                        | 0 / 19 (0.00%)<br>0                                                                                                                                        | 0 / 5 (0.00%)<br>0                                                                                                         |

|                                                                                 |                     |                     |                     |
|---------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)              | 1 / 23 (4.35%)<br>1 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Investigations                                                                  |                     |                     |                     |
| Blood iron increased<br>subjects affected / exposed<br>occurrences (all)        | 0 / 23 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |
| Blood urinc acid increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 23 (4.35%)<br>1 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Hyperuricemia<br>subjects affected / exposed<br>occurrences (all)               | 1 / 23 (4.35%)<br>1 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Serum amylase increased<br>subjects affected / exposed<br>occurrences (all)     | 1 / 23 (4.35%)<br>1 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Serum lipase increased<br>subjects affected / exposed<br>occurrences (all)      | 2 / 23 (8.70%)<br>2 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Injury, poisoning and procedural complications                                  |                     |                     |                     |
| Fall<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 23 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Injection site inflammation<br>subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0 | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Subarachonoid hemorrhage<br>subjects affected / exposed<br>occurrences (all)    | 0 / 23 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |
| Traumatic pneumothorax<br>subjects affected / exposed<br>occurrences (all)      | 0 / 23 (0.00%)<br>0 | 0 / 19 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |
| Cardiac disorders                                                               |                     |                     |                     |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 23 (4.35%)<br>1 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |

|                                      |                 |                 |                |
|--------------------------------------|-----------------|-----------------|----------------|
| Nervous system disorders             |                 |                 |                |
| Dizziness postural                   |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0              |
| Gait disturbance                     |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0              |
| Headache                             |                 |                 |                |
| subjects affected / exposed          | 3 / 23 (13.04%) | 2 / 19 (10.53%) | 0 / 5 (0.00%)  |
| occurrences (all)                    | 4               | 4               | 0              |
| Paresthesia                          |                 |                 |                |
| subjects affected / exposed          | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0               | 1               | 0              |
| Sensory disturbance                  |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0              |
| Blood and lymphatic system disorders |                 |                 |                |
| Anemia                               |                 |                 |                |
| subjects affected / exposed          | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  | 1 / 5 (20.00%) |
| occurrences (all)                    | 0               | 1               | 1              |
| Leukocytosis                         |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0              |
| Monocytosis                          |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 2               | 0               | 0              |
| Neutrophilia                         |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0              |
| Eye disorders                        |                 |                 |                |
| Dry eye                              |                 |                 |                |
| subjects affected / exposed          | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0              |
| Vision blurred                       |                 |                 |                |
| subjects affected / exposed          | 2 / 23 (8.70%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 3               | 0               | 0              |
| Gastrointestinal disorders           |                 |                 |                |

|                                 |                 |                |                |
|---------------------------------|-----------------|----------------|----------------|
| Abdominal pain upper            |                 |                |                |
| subjects affected / exposed     | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 2               | 0              | 0              |
| Anal fissure                    |                 |                |                |
| subjects affected / exposed     | 2 / 23 (8.70%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 2               | 0              | 0              |
| Colitis                         |                 |                |                |
| subjects affected / exposed     | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 1               | 0              | 0              |
| Constipation                    |                 |                |                |
| subjects affected / exposed     | 8 / 23 (34.78%) | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 8               | 0              | 0              |
| Diarrhea                        |                 |                |                |
| subjects affected / exposed     | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 1               | 0              | 0              |
| Diverticulosis                  |                 |                |                |
| subjects affected / exposed     | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 1               | 0              | 0              |
| Gastroesophageal reflux disease |                 |                |                |
| subjects affected / exposed     | 0 / 23 (0.00%)  | 0 / 19 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)               | 0               | 0              | 1              |
| Haemorrhoids                    |                 |                |                |
| subjects affected / exposed     | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 1               | 0              | 0              |
| Heartburn                       |                 |                |                |
| subjects affected / exposed     | 0 / 23 (0.00%)  | 1 / 19 (5.26%) | 1 / 5 (20.00%) |
| occurrences (all)               | 0               | 1              | 1              |
| Ileal ulcer                     |                 |                |                |
| subjects affected / exposed     | 1 / 23 (4.35%)  | 0 / 19 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)               | 1               | 0              | 0              |
| Mouth ulceration                |                 |                |                |
| subjects affected / exposed     | 0 / 23 (0.00%)  | 0 / 19 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)               | 0               | 0              | 1              |
| Nausea                          |                 |                |                |
| subjects affected / exposed     | 0 / 23 (0.00%)  | 0 / 19 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)               | 0               | 0              | 1              |

|                                                                         |                      |                     |                     |
|-------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| Periodontal disease<br>subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders                                  |                      |                     |                     |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)            | 1 / 23 (4.35%)<br>1  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Pemphigoid<br>subjects affected / exposed<br>occurrences (all)          | 0 / 23 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)            | 1 / 23 (4.35%)<br>1  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                | 5 / 23 (21.74%)<br>6 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Endocrine disorders                                                     |                      |                     |                     |
| Diabetes mellitus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 23 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders                         |                      |                     |                     |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)          | 3 / 23 (13.04%)<br>3 | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)           | 2 / 23 (8.70%)<br>2  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)           | 3 / 23 (13.04%)<br>3 | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)            | 0 / 23 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Fracture<br>subjects affected / exposed<br>occurrences (all)            | 0 / 23 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |

|                              |                 |                 |                |
|------------------------------|-----------------|-----------------|----------------|
| Heaviness in extremities     |                 |                 |                |
| subjects affected / exposed  | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 1               | 0               | 0              |
| Intervertebral disc disorder |                 |                 |                |
| subjects affected / exposed  | 2 / 23 (8.70%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 2               | 0               | 0              |
| Knee pain                    |                 |                 |                |
| subjects affected / exposed  | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 0               | 1               | 0              |
| Lumbar pain                  |                 |                 |                |
| subjects affected / exposed  | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)            | 1               | 0               | 1              |
| Muscular weakness            |                 |                 |                |
| subjects affected / exposed  | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 1               | 0               | 0              |
| Myalgia                      |                 |                 |                |
| subjects affected / exposed  | 6 / 23 (26.09%) | 1 / 19 (5.26%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 6               | 1               | 0              |
| Rib fracture                 |                 |                 |                |
| subjects affected / exposed  | 0 / 23 (0.00%)  | 0 / 19 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)            | 0               | 0               | 1              |
| Shoulder pain                |                 |                 |                |
| subjects affected / exposed  | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 1               | 0               | 0              |
| Spinal osteoarthritis        |                 |                 |                |
| subjects affected / exposed  | 1 / 23 (4.35%)  | 0 / 19 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 1               | 0               | 0              |
| Infections and infestations  |                 |                 |                |
| COVID-19                     |                 |                 |                |
| subjects affected / exposed  | 2 / 23 (8.70%)  | 4 / 19 (21.05%) | 0 / 5 (0.00%)  |
| occurrences (all)            | 2               | 4               | 0              |
| Common cold                  |                 |                 |                |
| subjects affected / exposed  | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  | 0 / 5 (0.00%)  |
| occurrences (all)            | 0               | 1               | 0              |
| Localised infection          |                 |                 |                |



|                                                                                       |                      |                     |                     |
|---------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                      | 0 / 23 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |
| Oral infection<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 23 (4.35%)<br>1  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 23 (4.35%)<br>1  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 0 / 23 (0.00%)<br>0  | 0 / 19 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |
| Metabolism and nutrition disorders                                                    |                      |                     |                     |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 23 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Hypercholesterolemia<br>subjects affected / exposed<br>occurrences (all)              | 3 / 23 (13.04%)<br>3 | 1 / 19 (5.26%)<br>2 | 0 / 5 (0.00%)<br>0  |
| Hypertriglyceridemia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 23 (4.35%)<br>1  | 1 / 19 (5.26%)<br>3 | 0 / 5 (0.00%)<br>0  |
| Hypomagnesemia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 23 (4.35%)<br>1  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Spinal flattening<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 23 (4.35%)<br>1  | 0 / 19 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 05 April 2019 | <ul style="list-style-type: none"><li>- An error was found in the calculation of the total number of weeks with and without treatment with the study medication (being 28-day cycles, the correct number is 48 weeks per year instead of 52) that affects the primary and secondary objectives.</li><li>- Discrepancies found between the study calendar tables and the protocol text.</li><li>-Update of CTCAE from version 4.03 to 5.0 (has been released and will be used for the study).</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study had a small sample size (23 patients), limiting generalizability. The single-arm design prevents direct comparisons with alternative treatment discontinuation strategies. The maximum follow-up was 96 weeks, which may not be sufficient.

Notes: