



Clinical trial results:

An Open-Label, Randomized, Multicenter Phase 2 Trial of Dasatinib (SPRYCEL®) vs. Dasatinib plus Smoothen Antagonist (BMS-833923) in the Treatment of Subjects with Newly Diagnosed Chronic Phase Philadelphia Chromosome Positive CML

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2011-000083-10 |
| Trial protocol | ES DE FI BE |
| Global end of trial date | 25 January 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 09 February 2017 |
| First version publication date | 09 February 2017 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | CA180-363 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01357655 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Parc de l'Alliance, Avenue de Finlande, 8, Braine l'Alleud, Belgium, 1420 |
| Public contact | EU Study Start-up Unit, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com |
| Scientific contact | EU Study Start-up Unit, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 January 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 January 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare response rates in newly diagnosed CP CML subjects treated with dasatinib plus BMS-833923 versus dasatinib alone.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 15 July 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Poland: 24 |
| Country: Number of subjects enrolled | Spain: 7 |
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Finland: 4 |
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | United States: 13 |
| Country: Number of subjects enrolled | Canada: 1 |
| Country: Number of subjects enrolled | Argentina: 3 |
| Worldwide total number of subjects | 70 |
| EEA total number of subjects | 53 |

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) | 58 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 24 sites worldwide.

Pre-assignment

Screening details:

70 subjects were enrolled, 66 were treated. Reasons for non-treatment include 1 adverse event and 3 no longer met study criteria. Participants enrolled were only treated with Dasatinib. The Dasatinib + SMO antagonist arm did not have participants because a tolerable and recommended phase 2 dose of the SMO antagonist had not been determined.

Period 1

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

Arms

| | |
|-----------|-----------|
| Arm title | Dasatinib |
|-----------|-----------|

Arm description:

Subjects received dasatinib, 100 mg, tablet, orally, once daily for approximately 1 year until the study was terminated prematurely.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | BMS-354825 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered with dasatinib 20 mg or 50 mg tablets orally once daily (QD) to make the total daily dose of 100 mg for up to 1 year. The study was terminated prematurely.

| Number of subjects in period 1 ^[1] | Dasatinib |
|---|-----------|
| Started | 66 |
| Completed | 0 |
| Not completed | 66 |
| Consent withdrawn by subject | 1 |
| Maximum Clinical Benefit | 2 |
| Adverse Event Unrelated to Study Drug | 3 |
| Study Drug Toxicity | 11 |
| Lost to follow-up | 2 |
| Reason Unspecified | 1 |
| Administrative Reason by Sponsor | 45 |
| Disease Progression | 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: Out of 70 subjects who were enrolled, 66 subjects received at least 1 dose of dasatinib.

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|------------------------|---------------|-------|--|
| Number of subjects | 66 | 66 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 18-64 years | 54 | 54 | |
| 65 years and over | 12 | 12 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 27 | 27 | |
| Male | 39 | 39 | |

End points

End points reporting groups

| | |
|--|-----------|
| Reporting group title | Dasatinib |
| Reporting group description: | |
| Subjects received dasatinib, 100 mg, tablet, orally, once daily for approximately 1 year until the study was terminated prematurely. | |

Primary: Number of Subjects With Major Molecular Response

| | |
|-----------------|---|
| End point title | Number of Subjects With Major Molecular Response ^[1] |
|-----------------|---|

End point description:

Major molecular response (MMR) was assessed using BCR-ABL transcript levels measured by real-time quantitative polymerase chain reaction (qPCR). MMR was defined as a ratio BCR-ABL/ABL $\leq 0.1\%$ on the international scale (ie, at least 3 log reduction from a standardized baseline value). Efficacy Sample: all treated subjects with at least one assessment on treatment. Number of subjects with MMR by timepoint are cumulative.

Subjects enrolled in this trial could not be randomized to the Dasatinib + SMO antagonist arm because no recommended phase 2 dose of the SMO antagonist could be determined (in a separate trial).

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

End point timeframe:

Baseline up to 12 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this end-point.

| End point values | Dasatinib | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 64 | | | |
| Units: subjects | | | | |
| Baseline | 1 | | | |
| 3 Months | 9 | | | |
| 6 Months | 30 | | | |
| 12 Months | 34 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Molecular Response at Any Time

| | |
|-----------------|---|
| End point title | Complete Molecular Response at Any Time |
|-----------------|---|

End point description:

The study was terminated prior to data collection for this endpoint.

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

End point timeframe:

Baseline to End of study (approximately 48 months)

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | Dasatinib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: participants | | | | |

Notes:

[2] - The study was terminated prior to data collection for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival, Measured by the Time From Start of Treatment to Progression or Death

| | |
|-----------------|---|
| End point title | Progression-free Survival, Measured by the Time From Start of Treatment to Progression or Death |
|-----------------|---|

End point description:

The study was terminated prior to data collection for this endpoint.

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

End point timeframe:

Baseline to End of study (approximately 48 months)

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | Dasatinib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[3] | | | |
| Units: months | | | | |
| number (not applicable) | | | | |

Notes:

[3] - The study was terminated prior to data collection for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival, Measured by the Time From Start of Treatment to Progression, Death or Treatment Discontinuation

| | |
|-----------------|--|
| End point title | Event-free Survival, Measured by the Time From Start of Treatment to Progression, Death or Treatment Discontinuation |
|-----------------|--|

End point description:

The study was terminated prior to data collection for this endpoint.

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

End point timeframe:

Baseline to End of study (approximately 48 months)

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | Dasatinib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[4] | | | |
| Units: months | | | | |
| number (not applicable) | | | | |

Notes:

[4] - The study was terminated prior to data collection for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Transformation-free Survival Measured by the Time From Start of Treatment to Criteria for Accelerated or Blast Phase CML Are Met and Death

| | |
|-----------------|--|
| End point title | Transformation-free Survival Measured by the Time From Start of Treatment to Criteria for Accelerated or Blast Phase CML Are Met and Death |
|-----------------|--|

End point description:

The study was terminated prior to data collection for this endpoint.

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

End point timeframe:

Baseline to End of study (approximately 48 months)

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | Dasatinib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[5] | | | |
| Units: months | | | | |
| number (not applicable) | | | | |

Notes:

[5] - The study was terminated prior to data collection for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Experiencing Serious Adverse Events (SAE), Drug-Related Adverse Event (AE), AE Leading to Discontinuation, and Death

| | |
|-----------------|---|
| End point title | Number of Subjects Experiencing Serious Adverse Events (SAE), Drug-Related Adverse Event (AE), AE Leading to Discontinuation, and Death |
|-----------------|---|

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/ incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Drug-related=having certain, probable, possible, or missing relationship to study drug. All Treated

Subjects.

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

End point timeframe:

From date of first dose of study treatment up to the date of the last dose plus 30 days (approximately 49 months)

| | | | | |
|-------------------------------|-----------------|--|--|--|
| End point values | Dasatinib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: subjects | | | | |
| SAE | 18 | | | |
| Drug-Related AE | 56 | | | |
| Death | 2 | | | |
| AE Leading to Discontinuation | 14 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On study adverse events: adverse events with onset on or after the first date of study treatment and on or prior to the last day of study treatment plus 30 days (approximately 49 months). All treated subjects.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Dasatinib |
|-----------------------|-----------|

Reporting group description:

Subjects received dasatinib, 100 mg, tablet, orally, once daily for approximately 1 year until the study was terminated prematurely.

| Serious adverse events | Dasatinib | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 66 (27.27%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Ovarian neoplasm | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal cancer | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac tamponade | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 66 (3.03%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|----------------|--|--|
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Amaurosis fugax | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Apical granuloma | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 2 / 66 (3.03%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Volvulus | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 2 / 66 (3.03%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 5 / 66 (7.58%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Liver abscess | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vaginal abscess | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Dasatinib | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 61 / 66 (92.42%) | | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 5 | | |
| Weight increased | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 5 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 7 / 66 (10.61%) | | |
| occurrences (all) | 7 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 27 / 66 (40.91%) | | |
| occurrences (all) | 34 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 20 / 66 (30.30%) | | |
| occurrences (all) | 35 | | |
| Leukopenia | | | |
| subjects affected / exposed | 8 / 66 (12.12%) | | |
| occurrences (all) | 19 | | |
| Neutropenia | | | |
| subjects affected / exposed | 14 / 66 (21.21%) | | |
| occurrences (all) | 54 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 17 / 66 (25.76%) | | |
| occurrences (all) | 45 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 13 / 66 (19.70%) | | |
| occurrences (all) | 21 | | |
| Chest pain | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 6 / 66 (9.09%) | | |
| occurrences (all) | 7 | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 66 (12.12%) | | |
| occurrences (all) | 9 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 5 | | |
| Pyrexia | | | |
| subjects affected / exposed | 10 / 66 (15.15%) | | |
| occurrences (all) | 13 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 66 (7.58%) | | |
| occurrences (all) | 8 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 4 | | |
| Constipation | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 4 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 18 / 66 (27.27%) | | |
| occurrences (all) | 31 | | |
| Nausea | | | |
| subjects affected / exposed | 14 / 66 (21.21%) | | |
| occurrences (all) | 21 | | |
| Vomiting | | | |
| subjects affected / exposed | 13 / 66 (19.70%) | | |
| occurrences (all) | 14 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 12 / 66 (18.18%) | | |
| occurrences (all) | 12 | | |
| Dyspnoea | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea exertional</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pleural effusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 66 (15.15%)</p> <p>16</p> <p>4 / 66 (6.06%)</p> <p>4</p> <p>4 / 66 (6.06%)</p> <p>4</p> <p>7 / 66 (10.61%)</p> <p>9</p> <p>9 / 66 (13.64%)</p> <p>26</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Acne</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 66 (6.06%)</p> <p>4</p> <p>11 / 66 (16.67%)</p> <p>13</p> | | |
| <p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 66 (6.06%)</p> <p>4</p> <p>6 / 66 (9.09%)</p> <p>7</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscle spasms</p> | <p>7 / 66 (10.61%)</p> <p>10</p> <p>5 / 66 (7.58%)</p> <p>5</p> | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 6 / 66 (9.09%) 10 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 6 / 66 (9.09%) 7 | | |
| Infections and infestations | | | |
| Gastroenteritis subjects affected / exposed occurrences (all) | 6 / 66 (9.09%) 6 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 5 / 66 (7.58%) 7 | | |
| Pharyngitis subjects affected / exposed occurrences (all) | 4 / 66 (6.06%) 6 | | |
| Sinusitis subjects affected / exposed occurrences (all) | 4 / 66 (6.06%) 4 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 8 / 66 (12.12%) 8 | | |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 4 / 66 (6.06%) 5 | | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 5 / 66 (7.58%) 9 | | |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 4 / 66 (6.06%) 13 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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 was terminated early as the overall tolerability of the SMO-antagonist observed in a Phase 1 study of dasatinib plus SMO-antagonist was considered unacceptable in the newly diagnosed CML population. |
|--|

Notes: