



## Clinical trial results:

### A Multicenter Phase 2 Study of Single-agent Filanesib (ARRY-520) in Patients With Advanced Multiple Myeloma

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2014-001051-23    |
| Trial protocol           | GB DE ES GR BE FR |
| Global end of trial date | 12 September 2017 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 06 January 2018 |
| First version publication date | 06 January 2018 |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | ARRAY-520-215 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02092922 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Array BioPharma Inc.   |
| Sponsor organisation address | 3200 Walnut Street, Boulder, Colorado, United States, 80301  |
| Public contact               | Teri Whisenand, Array BioPharma Inc., 001 3033861141, <a href="mailto:teri.whisenand@arraybiopharma.com">teri.whisenand@arraybiopharma.com</a> |
| Scientific contact           | Teri Whisenand, Array BioPharma Inc., 001 3033861141, <a href="mailto:teri.whisenand@arraybiopharma.com">teri.whisenand@arraybiopharma.com</a> |

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:

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**Results analysis stage**

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 05 February 2016  |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 05 February 2016  |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 12 September 2017 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

Main objective of the trial:

Estimate the objective response rate (ORR) for patients with low Baseline alpha 1-acid glycoprotein (AAG)

Protection of trial subjects:

Approval by the medical ethics committee (EC) and competent authority.

Participation in the study was voluntary and subject to the required patient information and informed consent procedures approved by the EC.

Strict in- and exclusion criteria to assure exclusion of vulnerable participants.

GCP trained staff.

Background therapy:

Filgrastim prophylaxis: Administered as a single daily subcutaneous (SC) bolus injection per the local product prescribing information and institutional guidelines, starting on Day 3 and on Day 17 (each time for a total of 5 to 7 days).

Prophylactic filgrastim allows the administration of higher filanesib doses, providing management of the hematologic effects associated with filanesib exposure and prevention of their complications.

Evidence for comparator:

N/A

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 16 April 2014 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Spain: 13         |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Belgium: 10       |
| Country: Number of subjects enrolled | France: 18        |
| Country: Number of subjects enrolled | Germany: 28       |
| Country: Number of subjects enrolled | Greece: 7         |
| Country: Number of subjects enrolled | United States: 67 |
| Country: Number of subjects enrolled | Canada: 7         |
| Worldwide total number of subjects   | 154               |
| EEA total number of subjects         | 80                |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                      | 69 |
| From 65 to 84 years                       | 85 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Period: 16 April 2014 to 28 July 2015

Territory: Belgium, Canada, France, Germany, Greece, Spain, United Kingdom, United States

### Pre-assignment

Screening details:

Screening evaluation included: Obtain written informed consent, record current and past medical history along with all transfusions/plasmaphereses administered, collect histopathologic confirmation of the diagnosis of multiple myeloma, record all prior treatments for multiple myeloma.

A total of 215 subjects were screened

### Period 1

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

Blinding implementation details:

N/A

### Arms

|           |                         |
|-----------|-------------------------|
| Arm title | Filanesib 1.5 mg/m2/day |
|-----------|-------------------------|

Arm description:

Filanesib 1.5 mg/m2/day administered IV as a 1-hour ( $\pm$  10-minute) infusion on Days 1, 2, 15 and 16.

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | Filanesib                         |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Powder for solution for injection |
| Routes of administration               | Intravenous use                   |

Dosage and administration details:

Per 28-day cycle: 1.5 mg/m2/day administered IV as a 1-hour ( $\pm$  10-minute) infusion on Days 1, 2, 15 and 16.

| Number of subjects in period 1 | Filanesib 1.5 mg/m2/day |
|--------------------------------|-------------------------|
| Started                        | 154                     |
| Completed                      | 151                     |
| Not completed                  | 3                       |
| Subjects not treated           | 3                       |

## Baseline characteristics

### Reporting groups

|                                |                                |
|--------------------------------|--------------------------------|
| Reporting group title          | Overall trial (overall period) |
| Reporting group description: - |                                |

| Reporting group values | Overall trial (overall period) | Total |  |
|------------------------|--------------------------------|-------|--|
| Number of subjects     | 154                            | 154   |  |
| Age categorical        |                                |       |  |
| Age group              |                                |       |  |
| Units: Subjects        |                                |       |  |
| Adults (18-64 years)   | 69                             | 69    |  |
| From 65-84 years       | 85                             | 85    |  |
| 85 years and over      | 0                              | 0     |  |
| Gender categorical     |                                |       |  |
| Gender                 |                                |       |  |
| Units: Subjects        |                                |       |  |
| Female                 | 63                             | 63    |  |
| Male                   | 91                             | 91    |  |

### Subject analysis sets

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | Intent-to-treat Set |
| Subject analysis set type  | Intention-to-treat  |

Subject analysis set description:

The intent-to-treat (ITT) Set included all patients who were enrolled for treatment.

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Safety Set      |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

The Safety Set (SS) included all patients who received 1 or more doses of filanesib.

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | Response Evaluable Set |
| Subject analysis set type  | Per protocol           |

Subject analysis set description:

The Response Evaluable Set (RES) included all patients in the SS who had at least 1 post-Baseline disease assessment or who discontinued from the study due to progressive disease (PD), AE or death prior to any disease assessment.

Patients whose disease at Baseline was not measurable or was not refractory to prior cancer treatments per protocol, and patients with other key protocol deviations may have been excluded from this set.

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | QTc Substudy Set   |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

The PK/QTc Substudy Set included all patients enrolled in the PK/QTc substudy who had at least 1 blood collection for PK with associated bioanalytical results and for whom at least 1 ECG result was obtained.

| Reporting group values | Intent-to-treat Set | Safety Set | Response Evaluable Set |
|------------------------|---------------------|------------|------------------------|
| Number of subjects     | 154                 | 151        | 145                    |
| Age categorical        |                     |            |                        |
| Age group              |                     |            |                        |
| Units: Subjects        |                     |            |                        |

|                      |    |  |  |
|----------------------|----|--|--|
| Adults (18-64 years) | 69 |  |  |
| From 65-84 years     | 85 |  |  |
| 85 years and over    | 0  |  |  |
| Gender categorical   |    |  |  |
| Gender               |    |  |  |
| Units: Subjects      |    |  |  |
| Female               | 63 |  |  |
| Male                 | 91 |  |  |

|                               |                  |  |  |
|-------------------------------|------------------|--|--|
| <b>Reporting group values</b> | QTc Substudy Set |  |  |
| Number of subjects            | 14               |  |  |
| Age categorical               |                  |  |  |
| Age group                     |                  |  |  |
| Units: Subjects               |                  |  |  |
| Adults (18-64 years)          |                  |  |  |
| From 65-84 years              |                  |  |  |
| 85 years and over             |                  |  |  |
| Gender categorical            |                  |  |  |
| Gender                        |                  |  |  |
| Units: Subjects               |                  |  |  |
| Female                        |                  |  |  |
| Male                          |                  |  |  |

## End points

### End points reporting groups

|  |                         |
|--|-------------------------|
| Reporting group title  | Filanesib 1.5 mg/m2/day |
| Reporting group description:<br>Filanesib 1.5 mg/m2/day administered IV as a 1-hour ( $\pm$ 10-minute) infusion on Days 1, 2, 15 and 16.   |                         |
| Subject analysis set title   | Intent-to-treat Set     |
| Subject analysis set type  | Intention-to-treat      |
| Subject analysis set description:<br>The intent-to-treat (ITT) Set included all patients who were enrolled for treatment.  |                         |
| Subject analysis set title   | Safety Set              |
| Subject analysis set type  | Safety analysis         |
| Subject analysis set description:<br>The Safety Set (SS) included all patients who received 1 or more doses of filanesib.  |                         |
| Subject analysis set title   | Response Evaluable Set  |
| Subject analysis set type  | Per protocol            |
| Subject analysis set description:<br>The Response Evaluable Set (RES) included all patients in the SS who had at least 1 post-Baseline disease assessment or who discontinued from the study due to progressive disease (PD), AE or death prior to any disease assessment.<br>Patients whose disease at Baseline was not measurable or was not refractory to prior cancer treatments per protocol, and patients with other key protocol deviations may have been excluded from this set. |                         |
| Subject analysis set title   | QTc Substudy Set        |
| Subject analysis set type  | Sub-group analysis      |
| Subject analysis set description:<br>The PK/QTc Substudy Set included all patients enrolled in the PK/QTc substudy who had at least 1 blood collection for PK with associated bioanalytical results and for whom at least 1 ECG result was obtained.   |                         |

### Primary: ORR in patients with low Baseline AAG

|   |  |
|---|--|
| End point title   | ORR in patients with low Baseline AAG <sup>[1]</sup> |
| End point description:<br>The ORR was calculated for each AAG subset (Low AAG, High AAG, Unknown AAG) and for all patients in the ITT Set as the proportion of patients whose overall best response by Independent Review (IR) was sCR, CR, very good partial response (VGPR) or partial response (PR). A 95% confidence interval (CI) for each ORR was calculated based on exact binomial distributions. |  |
| End point type  | Primary  |
| End point timeframe:<br>Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 $\pm$ 4 days of each cycle after Cycle 1).   |  |
| Notes:<br>[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.<br>Justification: No statistical analyses for this end point  |  |

| End point values            | Intent-to-treat Set  | Response Evaluable Set |  |  |
|-----------------------------|----------------------|------------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set   |  |  |
| Number of subjects analysed | 121                  | 116                    |  |  |
| Units: Subjects             |                      |                        |  |  |
| number (not applicable)     | 9                    | 9                      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: ORR in patients with high Baseline AAG

|                 |  |
|-----------------|--|
| End point title | ORR in patients with high Baseline AAG |
|-----------------|--|

End point description:

The ORR was calculated for each AAG subset (Low AAG, High AAG, Unknown AAG) and for all patients in the ITT Set as the proportion of patients whose overall best response by Independent Review (IR) was sCR, CR, very good partial response (VGPR) or partial response (PR). A 95% confidence interval (CI) for each ORR was calculated based on exact binomial distributions.

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

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1  $\pm$  4 days of each cycle after Cycle 1).

| End point values            | Intent-to-treat Set  | Response Evaluable Set |  |  |
|-----------------------------|----------------------|------------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set   |  |  |
| Number of subjects analysed | 26                   | 25                     |  |  |
| Units: Subjects             |                      |                        |  |  |
| number (not applicable)     | 1                    | 1                      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Best Response of sCR, CR, VGPR, or PR

|                 |   |
|-----------------|---|
| End point title | Duration of Best Response of sCR, CR, VGPR, or PR |
|-----------------|---|

End point description:

Duration of response is calculated for all patients achieving a sCR, CR, VGPR or PR and is defined as the time from first objective status assessment of sCR/CR/VGPR/PR to the time of first documented disease progression or death. A patient who initiates subsequent myeloma therapy after filanesib discontinuation and before documented disease progression will be censored at the last evaluable disease assessment prior to the start of the subsequent therapy. If a patient has not progressed, died or received subsequent myeloma therapy, the DOR will be censored on the day of the last evaluable disease assessment.

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

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1  $\pm$  4 days of each cycle after Cycle 1).



|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | Intent-to-treat Set  |  |  |  |
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 10                   |  |  |  |
| Units: months                 |                      |  |  |  |
| median (full range (min-max)) | 6.7 (1 to 11.5)      |  |  |  |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | Kaplan-Meier Plot Duration of Duration of Best Res/Kaplan- |
|-----------------------------------|--|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Best Response (TBR) of sCR, CR, VGPR, or PR

|   |   |
|---|---|
| End point title   | Time to Best Response (TBR) of sCR, CR, VGPR, or PR |
| End point description:<br>Time to response for patients achieving a sCR, CR, VGPR or PR is defined as the time from first filanesib infusion to the time of first objective status assessment of sCR/CR/VGPR/PR |   |
| End point type  | Secondary   |
| End point timeframe:<br>Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 $\pm$ 4 days of each cycle after Cycle 1).                 |   |

|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | Intent-to-treat Set  |  |  |  |
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 10                   |  |  |  |
| Units: months                 |                      |  |  |  |
| median (full range (min-max)) | 4.2 (1 to 12.9)      |  |  |  |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | Kaplan-Meier Plot Time to Best Response of sCR, CR/Kaplan- |
|-----------------------------------|--|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Best Response (TBR) of MR

|  |                                   |
|--|-----------------------------------|
| End point title  | Time to Best Response (TBR) of MR |
| End point description:<br>Time to response for patients achieving an MR is defined as the time from first filanesib infusion to the time of first objective status assessment of MR. |                                   |

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1). |           |

|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | Intent-to-treat Set  |  |  |  |
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 7                    |  |  |  |
| Units: months                 |                      |  |  |  |
| median (full range (min-max)) | 4.4 (1.1 to 9)       |  |  |  |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | Kaplan-Meier Plot Time to Best Response of MR/Kaplan-Meier |
|-----------------------------------|--|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical Benefit Rate (CBR)

|   |                             |
|---|-----------------------------|
| End point title   | Clinical Benefit Rate (CBR) |
| End point description:  |                             |
| Clinical benefit rate is defined as the proportion of patients who achieve ORR or MR (i.e., sCR, CR, VGPR, PR or MR).   |                             |
| End point type  | Secondary                   |
| End point timeframe:  |                             |
| Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1 ± 4 days of each cycle after Cycle 1). |                             |

|                             |                      |                        |  |  |
|-----------------------------|----------------------|------------------------|--|--|
| <b>End point values</b>     | Intent-to-treat Set  | Response Evaluable Set |  |  |
| Subject group type          | Subject analysis set | Subject analysis set   |  |  |
| Number of subjects analysed | 154                  | 145                    |  |  |
| Units: Subjects             |                      |                        |  |  |
| number (not applicable)     | 17                   | 17                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Disease Control Rate (DCR)

|                 |                            |
|-----------------|----------------------------|
| End point title | Disease Control Rate (DCR) |
|-----------------|----------------------------|

End point description:

The disease control rate (DCR) was calculated for each AAG subset and for all patients as the proportion of patients who achieved a best overall response by IR of sCR, CR, VGPR, PR, MR or stable disease (SD)  $\geq 8$  weeks in duration; 95% CIs calculated for ORR and DCR were based on exact binomial distributions.

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

End point timeframe:

Blood and/or urine disease assessments are to be performed approximately every 28 days during the treatment period (on Day 1  $\pm$  4 days of each cycle after Cycle 1).

| End point values            | Intent-to-treat Set  | Response Evaluable Set |  |  |
|-----------------------------|----------------------|------------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set   |  |  |
| Number of subjects analysed | 154                  | 145                    |  |  |
| Units: Subjects             |                      |                        |  |  |
| number (not applicable)     | 27                   | 26                     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS)

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

End point description:

Progression-free survival is defined as the time from first filanesib infusion to the first documented disease progression or death due to any cause. The date of progression can be the date of PD (for patients not meeting sCR/CR criteria), relapse from sCR/CR if meeting the criteria for progression, or clinical progression. A patient who initiates subsequent myeloma therapy after filanesib discontinuation and before documented disease progression will be censored at the last evaluable disease assessment prior to the start of the subsequent therapy. If a patient has not progressed, died or received subsequent myeloma therapy, the PFS will be censored on the day of the last evaluable disease assessment.

Median PFS and approximate 95% confidence intervals are estimated using Kaplan-Meier PFS techniques.

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

End point timeframe:

Time from first filanesib infusion to the first documented disease progression or death due to any cause

| End point values              | Intent-to-treat Set  | Intent-to-treat Set  |  |  |
|-------------------------------|----------------------|----------------------|--|--|
| Subject group type            | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed   | 154                  | 154                  |  |  |
| Units: months                 |                      |                      |  |  |
| median (full range (min-max)) | 2.1 (0 to 15.2)      | 2.1 (0 to 15.2)      |  |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | Kaplan-Meier Plot of progression-free survival/Kaplan-Meier |
|-----------------------------------|---|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Next Treatment (TNT)

|                 |                              |
|-----------------|------------------------------|
| End point title | Time to Next Treatment (TNT) |
|-----------------|------------------------------|

End point description:

Time to next treatment is calculated for all patients and is defined as the time from first filanesib infusion to the time of first subsequent documented myeloma therapy. Patients who have not received subsequent therapy at the time of this analysis (end of study) have been censored at the date of last contact or death due to any cause. Median TNT and approximate 95% confidence intervals are estimated using Kaplan-Meier PFS techniques.

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

End point timeframe:

Time from first filanesib infusion to the time of first subsequent documented myeloma therapy

|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | Intent-to-treat Set  |  |  |  |
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 254                  |  |  |  |
| Units: months                 |                      |  |  |  |
| median (full range (min-max)) | 3.3 (0 to 15.4)      |  |  |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | Kaplan-Meier Plot of time to next treatment (TNT)/Kaplan- |
|-----------------------------------|---|

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Overall trial period

Adverse event reporting additional description:

All subjects who were enrolled in the study and received at least one dose of study drug were included in the Safety Set

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Filanesib 1.5 mg/m2/day |
|-----------------------|-------------------------|

Reporting group description:

Filanesib 1.5 mg/m2/day administered IV as a 1-hour ( $\pm$  10-minute) infusion on Days 1, 2, 15 and 16.

| Serious adverse events  | Filanesib 1.5 mg/m2/day |  |  |
|---|-------------------------|--|--|
| Total subjects affected by serious adverse events                   |                         |  |  |
| subjects affected / exposed   | 43 / 151 (28.48%)       |  |  |
| number of deaths (all causes)                                       | 16                      |  |  |
| number of deaths resulting from adverse events                      | 6                       |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                         |  |  |
| Acute myeloid leukaemia   |                         |  |  |
| subjects affected / exposed   | 1 / 151 (0.66%)         |  |  |
| occurrences causally related to treatment / all                     | 1 / 1                   |  |  |
| deaths causally related to treatment / all                          | 1 / 1                   |  |  |
| Vascular disorders  |                         |  |  |
| Deep vein thrombosis  |                         |  |  |
| subjects affected / exposed   | 1 / 151 (0.66%)         |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                   |  |  |
| deaths causally related to treatment / all                          | 0 / 0                   |  |  |
| Hypotension   |                         |  |  |
| subjects affected / exposed   | 1 / 151 (0.66%)         |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                   |  |  |
| deaths causally related to treatment / all                          | 0 / 0                   |  |  |
| Hypovolaemic shock  |                         |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                          | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| General disorders and administration site conditions |                 |  |  |
| Pyrexia  |                 |  |  |
| subjects affected / exposed                          | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders      |                 |  |  |
| Epistaxis  |                 |  |  |
| subjects affected / exposed                          | 2 / 151 (1.32%) |  |  |
| occurrences causally related to treatment / all      | 1 / 2           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Respiratory failure                                  |                 |  |  |
| subjects affected / exposed                          | 2 / 151 (1.32%) |  |  |
| occurrences causally related to treatment / all      | 0 / 2           |  |  |
| deaths causally related to treatment / all           | 0 / 1           |  |  |
| Chronic obstructive pulmonary disease                |                 |  |  |
| subjects affected / exposed                          | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Dyspnoea   |                 |  |  |
| subjects affected / exposed                          | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Pleural effusion                                     |                 |  |  |
| subjects affected / exposed                          | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Psychiatric disorders                                |                 |  |  |
| Depression   |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| <b>Investigations</b>                                 |                 |  |  |
| Platelet count decreased                              |                 |  |  |
| subjects affected / exposed                           | 2 / 151 (1.32%) |  |  |
| occurrences causally related to treatment / all       | 1 / 2           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Blood creatinine increased                            |                 |  |  |
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Urine output decreased                                |                 |  |  |
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| White blood cell count decreased                      |                 |  |  |
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 1 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| <b>Injury, poisoning and procedural complications</b> |                 |  |  |
| Fall  |                 |  |  |
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Femur fracture  |                 |  |  |
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Lower limb fracture                                   |                 |  |  |
| subjects affected / exposed                           | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |

|   |                                   |  |  |
|---|-----------------------------------|--|--|
| Wrong drug administered<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                     | 1 / 151 (0.66%)<br>0 / 1<br>0 / 0 |  |  |
| Cardiac disorders<br>Acute myocardial infarction<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all            | 3 / 151 (1.99%)<br>0 / 3<br>0 / 0 |  |  |
| Cardiac failure<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 3 / 151 (1.99%)<br>1 / 3<br>1 / 2 |  |  |
| Myocardial ischaemia<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 151 (0.66%)<br>0 / 1<br>0 / 1 |  |  |
| Nervous system disorders<br>Spinal cord compression<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 1 / 151 (0.66%)<br>0 / 1<br>0 / 0 |  |  |
| Blood and lymphatic system disorders<br>Febrile neutropenia<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 6 / 151 (3.97%)<br>6 / 6<br>0 / 0 |  |  |
| Haematopoietic thrombocytopenia<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 3 / 151 (1.99%)<br>2 / 3<br>0 / 0 |  |  |
| Anaemia   |                                   |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 2 / 151 (1.32%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Stomatitis                                      |                 |  |  |
| subjects affected / exposed                     | 2 / 151 (1.32%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Constipation                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal haemorrhage                    |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Inguinal hernia                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Hepatic haemorrhage                             |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| Dermatitis bullous                              |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Renal failure acute                             |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 3 / 151 (1.99%) |  |  |
| occurrences causally related to treatment / all | 1 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Renal failure                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Back pain                                       |                 |  |  |
| subjects affected / exposed                     | 2 / 151 (1.32%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal pain                            |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pathological fracture                           |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Spinal pain                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Pneumonia                                       |                 |  |  |
| subjects affected / exposed                     | 7 / 151 (4.64%) |  |  |
| occurrences causally related to treatment / all | 3 / 8           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Sepsis  |                 |  |  |
| subjects affected / exposed                     | 4 / 151 (2.65%) |  |  |
| occurrences causally related to treatment / all | 2 / 4           |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Septic shock                                    |                 |  |  |  |
| subjects affected / exposed                     | 2 / 151 (1.32%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Aspergillus infection                           |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Bronchitis                                      |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Bronchopneumonia                                |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Escherichia sepsis                              |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Herpes zoster                                   |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Influenza                                       |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Lower respiratory tract infection               |                 |  |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Lung infection                                  |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Meningitis                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Meningococcal sepsis                            |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neutropenic infection                           |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumococcal sepsis                             |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory tract infection                     |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Sinusitis                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Staphylococcal sepsis                           |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Upper respiratory tract infection               |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urinary tract infection                         |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Viral infection                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neutropenia                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Thrombocytopenia                                |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Atrioventricular block complete                 |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neutropenic colitis                             |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Oesophageal candidiasis                         |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Hyperuricaemia                                  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hyponatraemia                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 151 (0.66%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Filanesib 1.5 mg/m2/day |  |  |
|---|-------------------------|--|--|
| Total subjects affected by non-serious adverse events |                         |  |  |
| subjects affected / exposed                           | 106 / 151 (70.20%)      |  |  |
| Investigations  |                         |  |  |
| Blood creatinine increased                            |                         |  |  |
| subjects affected / exposed                           | 17 / 151 (11.26%)       |  |  |
| occurrences (all)                                     | 17                      |  |  |
| Neutrophil count decreased                            |                         |  |  |
| subjects affected / exposed                           | 14 / 151 (9.27%)        |  |  |
| occurrences (all)                                     | 14                      |  |  |
| Platelet count decreased                              |                         |  |  |
| subjects affected / exposed                           | 23 / 151 (15.23%)       |  |  |
| occurrences (all)                                     | 23                      |  |  |
| Weight decreased                                      |                         |  |  |
| subjects affected / exposed                           | 14 / 151 (9.27%)        |  |  |
| occurrences (all)                                     | 14                      |  |  |
| White blood cell count decreased                      |                         |  |  |
| subjects affected / exposed                           | 12 / 151 (7.95%)        |  |  |
| occurrences (all)                                     | 12                      |  |  |
| Vascular disorders                                    |                         |  |  |
| Hypertension  |                         |  |  |
| subjects affected / exposed                           | 9 / 151 (5.96%)         |  |  |
| occurrences (all)                                     | 9                       |  |  |
| Hypotension   |                         |  |  |

|   |                      |  |  |
|---|----------------------|--|--|
| subjects affected / exposed<br>occurrences (all)        | 9 / 151 (5.96%)<br>9 |  |  |
| Nervous system disorders                                |                      |  |  |
| Headache  |                      |  |  |
| subjects affected / exposed                             | 15 / 151 (9.93%)     |  |  |
| occurrences (all)                                       | 15                   |  |  |
| Dysgeusia   |                      |  |  |
| subjects affected / exposed                             | 8 / 151 (5.30%)      |  |  |
| occurrences (all)                                       | 8                    |  |  |
| Dizziness   |                      |  |  |
| subjects affected / exposed                             | 7 / 151 (4.64%)      |  |  |
| occurrences (all)                                       | 7                    |  |  |
| Blood and lymphatic system disorders                    |                      |  |  |
| Thrombocytopenia  |                      |  |  |
| subjects affected / exposed                             | 43 / 151 (28.48%)    |  |  |
| occurrences (all)                                       | 43                   |  |  |
| Anaemia   |                      |  |  |
| subjects affected / exposed                             | 72 / 151 (47.68%)    |  |  |
| occurrences (all)                                       | 72                   |  |  |
| Febrile neutropenia                                     |                      |  |  |
| subjects affected / exposed                             | 8 / 151 (5.30%)      |  |  |
| occurrences (all)                                       | 8                    |  |  |
| Neutropenia   |                      |  |  |
| subjects affected / exposed                             | 34 / 151 (22.52%)    |  |  |
| occurrences (all)                                       | 34                   |  |  |
| Leukopenia  |                      |  |  |
| subjects affected / exposed                             | 11 / 151 (7.28%)     |  |  |
| occurrences (all)                                       | 11                   |  |  |
| General disorders and administration<br>site conditions |                      |  |  |
| Fatigue   |                      |  |  |
| subjects affected / exposed                             | 37 / 151 (24.50%)    |  |  |
| occurrences (all)                                       | 37                   |  |  |
| Pyrexia   |                      |  |  |
| subjects affected / exposed                             | 23 / 151 (15.23%)    |  |  |
| occurrences (all)                                       | 23                   |  |  |
| Asthenia  |                      |  |  |

|   |                   |  |  |
|---|-------------------|--|--|
| subjects affected / exposed                     | 17 / 151 (11.26%) |  |  |
| occurrences (all)                               | 17                |  |  |
| Mucosal inflammation                            |                   |  |  |
| subjects affected / exposed                     | 7 / 151 (4.64%)   |  |  |
| occurrences (all)                               | 7                 |  |  |
| Oedema peripheral                               |                   |  |  |
| subjects affected / exposed                     | 12 / 151 (7.95%)  |  |  |
| occurrences (all)                               | 12                |  |  |
| Gastrointestinal disorders                      |                   |  |  |
| Stomatitis                                      |                   |  |  |
| subjects affected / exposed                     | 12 / 151 (7.95%)  |  |  |
| occurrences (all)                               | 12                |  |  |
| Nausea  |                   |  |  |
| subjects affected / exposed                     | 33 / 151 (21.85%) |  |  |
| occurrences (all)                               | 33                |  |  |
| Diarrhoea                                       |                   |  |  |
| subjects affected / exposed                     | 30 / 151 (19.87%) |  |  |
| occurrences (all)                               | 30                |  |  |
| Vomiting  |                   |  |  |
| subjects affected / exposed                     | 17 / 151 (11.26%) |  |  |
| occurrences (all)                               | 17                |  |  |
| Constipation                                    |                   |  |  |
| subjects affected / exposed                     | 19 / 151 (12.58%) |  |  |
| occurrences (all)                               | 19                |  |  |
| Respiratory, thoracic and mediastinal disorders |                   |  |  |
| Dyspnoea  |                   |  |  |
| subjects affected / exposed                     | 17 / 151 (11.26%) |  |  |
| occurrences (all)                               | 17                |  |  |
| Cough   |                   |  |  |
| subjects affected / exposed                     | 18 / 151 (11.92%) |  |  |
| occurrences (all)                               | 18                |  |  |
| Epistaxis                                       |                   |  |  |
| subjects affected / exposed                     | 16 / 151 (10.60%) |  |  |
| occurrences (all)                               | 16                |  |  |
| Oropharyngeal pain                              |                   |  |  |



|   |                   |  |  |
|---|-------------------|--|--|
| subjects affected / exposed                     | 7 / 151 (4.64%)   |  |  |
| occurrences (all)                               | 7                 |  |  |
| Nasal congestion                                |                   |  |  |
| subjects affected / exposed                     | 9 / 151 (5.96%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Skin and subcutaneous tissue disorders          |                   |  |  |
| Pruritus  |                   |  |  |
| subjects affected / exposed                     | 9 / 151 (5.96%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Musculoskeletal and connective tissue disorders |                   |  |  |
| Back pain                                       |                   |  |  |
| subjects affected / exposed                     | 25 / 151 (16.56%) |  |  |
| occurrences (all)                               | 25                |  |  |
| Bone pain                                       |                   |  |  |
| subjects affected / exposed                     | 23 / 151 (15.23%) |  |  |
| occurrences (all)                               | 23                |  |  |
| Pain in extremity                               |                   |  |  |
| subjects affected / exposed                     | 15 / 151 (9.93%)  |  |  |
| occurrences (all)                               | 15                |  |  |
| Arthralgia                                      |                   |  |  |
| subjects affected / exposed                     | 10 / 151 (6.62%)  |  |  |
| occurrences (all)                               | 10                |  |  |
| Musculoskeletal chest pain                      |                   |  |  |
| subjects affected / exposed                     | 10 / 151 (6.62%)  |  |  |
| occurrences (all)                               | 10                |  |  |
| Muscle spasms                                   |                   |  |  |
| subjects affected / exposed                     | 9 / 151 (5.96%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Musculoskeletal pain                            |                   |  |  |
| subjects affected / exposed                     | 9 / 151 (5.96%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Infections and infestations                     |                   |  |  |
| Pneumonia                                       |                   |  |  |
| subjects affected / exposed                     | 10 / 151 (6.62%)  |  |  |
| occurrences (all)                               | 10                |  |  |
| Respiratory tract infection                     |                   |  |  |

|   |                         |  |  |
|---|-------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                      | 8 / 151 (5.30%)<br>8    |  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 14 / 151 (9.27%)<br>14  |  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 7 / 151 (4.64%)<br>7    |  |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 7 / 151 (4.64%)<br>7    |  |  |
| Metabolism and nutrition disorders  |                         |  |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 26 / 151 (17.22%)<br>26 |  |  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                      | 20 / 151 (13.25%)<br>20 |  |  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 13 / 151 (8.61%)<br>13  |  |  |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)                    | 12 / 151 (7.95%)<br>12  |  |  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)                     | 8 / 151 (5.30%)<br>8    |  |  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 7 / 151 (4.64%)<br>7    |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment  |
|---------------|--|
| 05 March 2015 | <p>In order to make the study available to a larger group of appropriate patients, the platelet count required for study entry was reduced to <math>50 \times 10^9/L</math> for all patients, regardless of the % plasma cells in the bone marrow. This change is not expected to result in additional safety concerns, as the dose modification criteria relating to hematologic abnormalities (including thrombocytopenia) have not been changed.</p> <p>Additional substantive changes are as follows:</p> <ul style="list-style-type: none"><li>• The upper limit on filanesib dose based on body surface area (BSA) was removed, as it was not supported by safety or pharmacokinetics data to date.</li><li>• Acceptable methods of skeletal imaging were expanded to include whole-body low-dose computed tomography.</li><li>• Acceptable methods of plasmacytoma measurement were expanded to include physical examination.</li><li>• Recommendations regarding dose and duration of prophylactic filgrastim administration were added.</li><li>• Requirement for a 1-week duration between assessments to confirm PD was removed, as it is not required per IMWG criteria.</li><li>• Guidance regarding stability of drug product following reconstitution and dilution was updated.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported