



## Clinical trial results:

### Phase II, Open-Label, Randomized, Controlled Study of PM060184 in Advanced, Hormone Receptor Positive, HER2 negative Breast Cancer Patients in Third or Fourth Line Setting.

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-002395-24  |
| Trial protocol           | ES BE           |
| Global end of trial date | 30 October 2017 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 16 November 2018 |
| First version publication date | 16 November 2018 |

#### Trial information

##### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | PM60184-B-001-15 |
|-----------------------|------------------|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Pharma Mar, S.A.  |
| Sponsor organisation address | Avenida de los Reyes, 1 Polígono Industrial "La Mina", Colmenar Viejo, Madrid, Spain, 28770   |
| Public contact               | Clinical Development, Department of PharmaMar's Oncology., Business Unit., Pharma Mar, S.A., 34 91846 60 00, clinicaltrials@pharmamar.com |
| Scientific contact           | Clinical Development, Department of PharmaMar's Oncology., Business Unit., Pharma Mar, S.A., 34 91846 60 00, clinicaltrials@pharmamar.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                       | 03 October 2018 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 30 October 2017 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 30 October 2017 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To Evaluate the efficacy of PM060184 in terms of progression-free survival at 4 months (PFS4) in third or fourth line setting in the subset population of advanced, hormone receptor positive, human epidermal growth factor receptor 2 (HER2) negative, breast carcinoma

Protection of trial subjects:

The study was in compliance with ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

Primary antiemetic prophylaxis was compulsory prior to all PM060184 administrations. Standard treatment, according to ASCO guidelines, was administered:

- 5-HT3 antagonists (ondansetron 8 mg or equivalent).
- Steroids (dexamethasone 8 mg or equivalent).
- Both oral and i.v. formulations were allowed, following the local institutional standards.

If necessary, additional and/or extended antiemetic treatment could be considered (according to the Investigators' standard practice).

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 12 February 2016 |
| 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 | Spain: 22 |
| Worldwide total number of subjects   | 22        |
| EEA total number of subjects         | 22        |

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)      | 18 |
| From 65 to 84 years       | 4  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

At cutoff date, 22 patients had been included in the 1st stage: 21 were treated and evaluable for safety, and 18 were evaluable for the primary efficacy endpoint (PFS4).

Patients enrollment between 12Feb2016 and 30Oct2017 (date of last F-Up, clinical cutoff) and corresponds to the 1st stage. All the patients were enrolled at 5 sites in Spain.

### Pre-assignment

Screening details:

Screening details:

IC Signed, Age  $\geq 18$ , Histologically diagnosis BC, Tumors HR+ & HER2-, 2-3 chemotherapy lines, Previous treatment anthracyclines & taxanes, ECOG: PS 0 or 1, Adequate marrow, liver and kidney function, Normal LVEF by ECHO or MUGA, Life expectancy  $\geq 3$  mo., Recovery grade  $\leq 1$  from any toxicity, Peripheral neuropathy grade  $\leq 1$  for AE, negative pre

### Period 1

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

Blinding implementation details:

Not blinded

### Arms

|           |          |
|-----------|----------|
| Arm title | PM060184 |
|-----------|----------|

Arm description:

The only drug administered and evaluated was PM060184, which was administered i.v. via a central line or a peripheral venous catheter (in 5 or 1-min administrations) at a dose of 9.3 mg/m<sup>2</sup> on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle).

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | PM060184                        |
| Investigational medicinal product code | PM060184                        |
| Other name                             |                                 |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

The only drug administered and evaluated was PM060184, which was administered i.v. via a central line or a peripheral venous catheter (in 5 or 1-min administrations) at a dose of 9.3 mg/m<sup>2</sup> on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle).

The drug substance PM060184-CD is a mixture of PM060184 and 2-hydroxypropyl- $\beta$ -cyclodextrin.

PM060184 drug product (DP) is provided as a sterile lyophilized powder for concentrate for solution for infusion with a strength of 15 mg of the active moiety PM060184.

Before use, the vials should be reconstituted with 6 mL of water for injection to give a solution containing 2.5 mg/mL of PM060184. PM060184 as 15-mg DP was developed for i.v. administration. Prior to administration, the reconstituted vials were further diluted with a dextrose 5% solution for infusion. Each 15-mg vial of PM060184 was a single-use vial. The diluted solution should be protected from light exposure.

| <b>Number of subjects in period 1</b> | PM060184 |
|---------------------------------------|----------|
| Started                               | 22       |
| Completed                             | 0        |
| Not completed                         | 22       |
| Clinical deterioration                | 1        |
| Never treated                         | 1        |
| Progressive disease                   | 12       |
| Treatment-related adverse event       | 2        |
| Patient refusal to treatment          | 6        |

## Baseline characteristics

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | PM060184 |
|-----------------------|----------|

Reporting group description:

The only drug administered and evaluated was PM060184, which was administered i.v. via a central line or a peripheral venous catheter (in 5 or 1-min administrations) at a dose of 9.3 mg/m<sup>2</sup> on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle).

| Reporting group values | PM060184 | Total |  |
|------------------------|----------|-------|--|
| Number of subjects     | 22       | 22    |  |
| Age categorical        |          |       |  |
| Units: Subjects        |          |       |  |
| 18-49                  | 11       | 11    |  |
| 50-69                  | 8        | 8     |  |
| ≥70                    | 3        | 3     |  |
| Age continuous         |          |       |  |
| Units: years           |          |       |  |
| median                 | 51       |       |  |
| full range (min-max)   | 36 to 76 | -     |  |
| Gender categorical     |          |       |  |
| Units: Subjects        |          |       |  |
| Female                 | 22       | 22    |  |
| Male                   | 0        | 0     |  |
| Race                   |          |       |  |
| Units: Subjects        |          |       |  |
| White                  | 21       | 21    |  |
| Other (Hispanic)       | 1        | 1     |  |
| ECOG PS                |          |       |  |
| Units: Subjects        |          |       |  |
| PS 0                   | 11       | 11    |  |
| PS 1                   | 11       | 11    |  |
| Stage at diagnosis     |          |       |  |
| Units: Subjects        |          |       |  |
| Stage I                | 1        | 1     |  |
| Stage IIA              | 8        | 8     |  |
| Stage IIB              | 2        | 2     |  |
| Stage IIIA             | 3        | 3     |  |
| Stage IIIC             | 2        | 2     |  |
| Stage IV               | 5        | 5     |  |
| Stage UK               | 1        | 1     |  |
| Primary tumor site     |          |       |  |
| Units: Subjects        |          |       |  |
| Bilateral              | 2        | 2     |  |
| Left                   | 11       | 11    |  |
| Right                  | 9        | 9     |  |
| Hystology type         |          |       |  |
| Units: Subjects        |          |       |  |
| Ductal                 | 22       | 22    |  |

|  |    |    |  |
|--|----|----|--|
| Histology grade  |    |    |  |
| G: Grade   |    |    |  |
| Units: Subjects  |    |    |  |
| G1: Well differentiated  | 2  | 2  |  |
| G2: Moderately differentiated  | 16 | 16 |  |
| G3: Poorly differentiated  | 2  | 2  |  |
| G4: Undifferentiated   | 1  | 1  |  |
| GX: Grade cannot be assessed   | 1  | 1  |  |
| Second breast cancer   |    |    |  |
| Units: Subjects  |    |    |  |
| Yes  | 1  | 1  |  |
| No   | 21 | 21 |  |
| Hormone Receptor   |    |    |  |
| Units: Subjects  |    |    |  |
| Both hormone receptors positive  | 17 | 17 |  |
| Estrogen positive  | 5  | 5  |  |
| HER2 negative  |    |    |  |
| FISH: fluorescence in situ hybridization   |    |    |  |
| Units: Subjects  |    |    |  |
| HercepTest   | 15 | 15 |  |
| HercepTest and FISH  | 7  | 7  |  |
| Ki67/MIB-1   |    |    |  |
| Units: Subjects  |    |    |  |
| <5%  | 2  | 2  |  |
| 5-10%  | 1  | 1  |  |
| >10  | 13 | 13 |  |
| ND/UK  | 6  | 6  |  |
| BRCA status  |    |    |  |
| Patient had BRCA2 mutation and no sites of measurable disease reported in the source documents, but she was never treated with PM060184 and was excluded from the analysis of efficacy and safety. |    |    |  |
| Units: Subjects  |    |    |  |
| No   | 3  | 3  |  |
| UK   | 18 | 18 |  |
| Yes  | 1  | 1  |  |
| Number of sites involved   |    |    |  |
| Units: Subjects  |    |    |  |
| 0 site   | 1  | 1  |  |
| 1 site   | 1  | 1  |  |
| 2 sites  | 8  | 8  |  |
| 3 sites  | 6  | 6  |  |
| 4 sites  | 3  | 3  |  |
| 5 sites  | 2  | 2  |  |
| 6 sites  | 1  | 1  |  |
| Peripheral neuropathy  |    |    |  |
| Units: Subjects  |    |    |  |
| No   | 15 | 15 |  |
| Yes  | 7  | 7  |  |
| Type of peripheral neuropathy  |    |    |  |
| Units: Subjects  |    |    |  |
| Both (motor and sensory)   | 3  | 3  |  |
| Sensory  | 4  | 4  |  |

|   |             |    |  |
|---|-------------|----|--|
| No peripheral neuropathy  | 15          | 15 |  |
| NCI-CTCAE grade   |             |    |  |
| According to the NCI-CTCAE v.4.   |             |    |  |
| Units: Subjects   |             |    |  |
| Grade 1   | 4           | 4  |  |
| Grade 2   | 3           | 3  |  |
| No peripheral neuropathy  | 15          | 15 |  |
| Prior radiotherapy  |             |    |  |
| Units: Subjects   |             |    |  |
| Yes   | 16          | 16 |  |
| No  | 6           | 6  |  |
| Prior surgery for primary treatment   |             |    |  |
| Units: Subjects   |             |    |  |
| Mastectomy  | 11          | 11 |  |
| Breast-conserving surgery   | 8           | 8  |  |
| No surgery  | 3           | 3  |  |
| Number of prior lines   |             |    |  |
| Units: Subjects   |             |    |  |
| 2 lines   | 2           | 2  |  |
| 3 lines   | 3           | 3  |  |
| 4 lines   | 4           | 4  |  |
| ≥5 lines  | 13          | 13 |  |
| Number of prior lines for advanced/metastatic disease   |             |    |  |
| Includes chemotherapy and hormonotherapy.   |             |    |  |
| Units: Subjects   |             |    |  |
| 2 lines   | 7           | 7  |  |
| 3 lines   | 5           | 5  |  |
| ≥5 lines  | 10          | 10 |  |
| Number of prior chemotherapy lines  |             |    |  |
| Includes neoadjuvant, adjuvant and advanced chemotherapy  |             |    |  |
| Units: Subjects   |             |    |  |
| 2 lines   | 4           | 4  |  |
| 3 lines   | 13          | 13 |  |
| 4 lines   | 4           | 4  |  |
| 5 lines   | 1           | 1  |  |
| Number of prior advanced chemotherapy lines   |             |    |  |
| Units: Subjects   |             |    |  |
| 2 lines   | 14          | 14 |  |
| 3 lines   | 8           | 8  |  |
| Best response to last prior therapy   |             |    |  |
| NE, not evaluable; PD, disease progression; PR, partial response; SD, stable disease; UK, unknown |             |    |  |
| Units: Subjects   |             |    |  |
| PR  | 4           | 4  |  |
| SD  | 11          | 11 |  |
| PD  | 4           | 4  |  |
| UK/NE   | 3           | 3  |  |
| Weight  |             |    |  |
| Units: Kg   |             |    |  |
| median  | 63.7        |    |  |
| full range (min-max)  | 48 to 109.5 | -  |  |



|   |                        |   |  |
|---|------------------------|---|--|
| Height<br>Units: cm<br>median<br>full range (min-max)   | 160<br>151 to 168      | - |  |
| BSA   |                        |   |  |
| BSA: Body Surface Area  |                        |   |  |
| Units: m2<br>median<br>full range (min-max)   | 1.6<br>1.6 to 2.2      | - |  |
| Time from first diagnosis to first PM060184 infusion  |                        |   |  |
| Data on 21 patients (one patient was never treated with PM060184)   |                        |   |  |
| Units: months<br>median<br>full range (min-max)   | 108.7<br>14.3 to 416.5 | - |  |
| Time from first diagnosis of advance disease to first PM060184 infusion   |                        |   |  |
| Data on 21 patients (one patient was never treated with PM060184)   |                        |   |  |
| Units: months<br>median<br>full range (min-max)   | 35.4<br>11.8 to 132.8  | - |  |
| Time from prior last progression before study entry   |                        |   |  |
| Patient signed informed consent on 20 September 2016. Although suspicion of disease progression was previous (20 August 2016), PD was confirmed through CT scan on 28 September 2016 and PM060184 treatment was started on 29 September 2016. |                        |   |  |
| Units: months<br>median<br>full range (min-max)   | 0.4<br>-0.3 to 1.5     | - |  |
| Time from stop date of last prior therapy to study entry  |                        |   |  |
| Units: months<br>median<br>full range (min-max)   | 0.7<br>0.2 to 2.4      | - |  |
| Number of sites involved  |                        |   |  |
| Units: Sites<br>median<br>full range (min-max)  | 3<br>0 to 6            | - |  |
| Number of prior lines   |                        |   |  |
| Units: Lines<br>median<br>full range (min-max)  | 5<br>2 to 8            | - |  |
| Number of prior lines for advanced/metastatic disease   |                        |   |  |
| Includes neoadjuvant, adjuvant and advanced chemotherapy  |                        |   |  |
| Units: Lines<br>median<br>full range (min-max)  | 3<br>2 to 7            | - |  |
| Number of prior chemotherapy lines  |                        |   |  |
| Includes neoadjuvant, adjuvant and advanced chemotherapy  |                        |   |  |
| Units: Lines<br>median<br>full range (min-max)  | 3<br>2 to 5            | - |  |
| Number of prior advanced  |                        |   |  |

|                           |             |   |  |
|---------------------------|-------------|---|--|
| chemotherapy lines        |             |   |  |
| Units: lines              |             |   |  |
| median                    | 2           |   |  |
| full range (min-max)      | 2 to 3      | - |  |
| Progression-free interval |             |   |  |
| Units: months             |             |   |  |
| median                    | 0.4         |   |  |
| full range (min-max)      | -0.3 to 1.5 | - |  |

## End points

### End points reporting groups

|   |          |
|---|----------|
| Reporting group title   | PM060184 |
| Reporting group description:  |          |
| The only drug administered and evaluated was PM060184, which was administered i.v. via a central line or a peripheral venous catheter (in 5 or 1-min administrations) at a dose of 9.3 mg/m <sup>2</sup> on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle). |          |

### Primary: Progression-free survival rate at four months (PFS4)

|  |   |
|--|---|
| End point title  | Progression-free survival rate at four months (PFS4) <sup>[1]</sup> |
| End point description:   |   |
| Progression-free survival rate at four months (PFS4), defined as the rate estimate of the percentage of patients who were alive and progression-free at 16 weeks (~4 months) after the first treatment administration. |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| Overall period   |   |

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: The threshold for proving antitumor activity (at least nine patients reaching PFS4) was not reached, the primary endpoint was unmet, and the study was closed without recruiting more patients in the first stage and without opening the second stage.

| End point values                 | PM060184            |  |  |  |
|----------------------------------|---------------------|--|--|--|
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 18 <sup>[2]</sup>   |  |  |  |
| Units: percentage                |                     |  |  |  |
| number (confidence interval 95%) |                     |  |  |  |
| Yes                              | 11.1 (1.4 to 34.7)  |  |  |  |
| No                               | 88.9 (65.3 to 98.6) |  |  |  |

Notes:

[2] - Four patients were not considered evaluable for efficacy

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival

|   |                  |
|---|------------------|
| End point title   | Overall Survival |
| End point description:  |                  |
| OS, defined as the time from the first day of treatment to the date of death or last contact. |                  |
| End point type  | Secondary        |
| End point timeframe:  |                  |
| Overall period  |                  |

|                                  |                   |  |  |  |
|----------------------------------|-------------------|--|--|--|
| <b>End point values</b>          | PM060184          |  |  |  |
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 18 <sup>[3]</sup> |  |  |  |
| Units: months                    |                   |  |  |  |
| median (confidence interval 95%) | 6.6 (4.5 to 999)  |  |  |  |

Notes:

[3] - Four patients were not considered evaluable for efficacy

999= not reached

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-free Survival

|   |                           |
|---|---------------------------|
| End point title   | Progression-free Survival |
| End point description:  |                           |
| PFS, defined as the time from the first day of study treatment to the day of negative efficacy assessment (progression or death) or last tumor evaluation |                           |
| PFS at 6 months (95% CI): 9.7% (0-27.4)   |                           |
| End point type  | Secondary                 |
| End point timeframe:  |                           |
| Overall period  |                           |

|                                  |                   |  |  |  |
|----------------------------------|-------------------|--|--|--|
| <b>End point values</b>          | PM060184          |  |  |  |
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 18 <sup>[4]</sup> |  |  |  |
| Units: months                    |                   |  |  |  |
| median (confidence interval 95%) | 1.9 (1.2 to 3.8)  |  |  |  |

Notes:

[4] - Four patients were not considered evaluable for efficacy

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Response Rate

|  |                       |
|--|-----------------------|
| End point title  | Overall Response Rate |
| End point description:   |                       |
| ORR, defined as the percentage of patients with objective response, either CR or PR according to the RECIST v.1.1 criteria |                       |
| CR, complete response; ORR, overall response rate; PD, disease progression; PR, partial response; SD, stable disease.      |                       |
| ORR (95% CI) 5.6% (0.1-27.3%)  |                       |
| Clinical benefit rate (CR+PR+SD ≥ 4 months) (95% CI) 16.7% (3.6-41.4%)   |                       |

Only one patient achieved a partial response, which lasted 1.9 months

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Overall period       |           |

|                             |                   |  |  |  |
|-----------------------------|-------------------|--|--|--|
| <b>End point values</b>     | PM060184          |  |  |  |
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 18 <sup>[5]</sup> |  |  |  |
| Units: subjects             |                   |  |  |  |
| PR                          | 1                 |  |  |  |
| SD                          | 8                 |  |  |  |
| PD                          | 9                 |  |  |  |

Notes:

[5] - Four patients were not considered evaluable for efficacy'

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Overall period

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | PM060184 |
|-----------------------|----------|

Reporting group description: -

| Serious adverse events                               | PM060184        |  |  |
|--|-----------------|--|--|
| Total subjects affected by serious adverse events    |                 |  |  |
| subjects affected / exposed                          | 4 / 21 (19.05%) |  |  |
| number of deaths (all causes)                        | 4               |  |  |
| number of deaths resulting from adverse events       | 0               |  |  |
| Surgical and medical procedures                      |                 |  |  |
| Wrist surgery  |                 |  |  |
| subjects affected / exposed                          | 1 / 21 (4.76%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Blood and lymphatic system disorders                 |                 |  |  |
| Neutropenia  |                 |  |  |
| subjects affected / exposed                          | 1 / 21 (4.76%)  |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Thrombocytopenia                                     |                 |  |  |
| subjects affected / exposed                          | 1 / 21 (4.76%)  |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| General disorders and administration site conditions |                 |  |  |
| Fatigue  |                 |  |  |
| subjects affected / exposed                          | 1 / 21 (4.76%)  |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |

|  |   |                |  |  |
|--|---|----------------|--|--|
| Gastrointestinal disorders<br>Constipation     | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | occurrences causally related to treatment / all | 0 / 1          |  |  |
|  | deaths causally related to treatment / all      | 0 / 0          |  |  |
| Intestinal obstruction                         | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | occurrences causally related to treatment / all | 1 / 1          |  |  |
|  | deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nausea   | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | occurrences causally related to treatment / all | 1 / 1          |  |  |
|  | deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting                                       | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | occurrences causally related to treatment / all | 1 / 1          |  |  |
|  | deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | occurrences causally related to treatment / all | 1 / 1          |  |  |
|  | deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations<br>Sepsis          | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | occurrences causally related to treatment / all | 0 / 1          |  |  |
|  | deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders<br>Anorexia | subjects affected / exposed                     | 1 / 21 (4.76%) |  |  |
|  | 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>                                   | PM060184          |  |  |
| Total subjects affected by non-serious adverse events               |                   |  |  |
| subjects affected / exposed   | 21 / 21 (100.00%) |  |  |
| Investigations  |                   |  |  |
| Alt increased   |                   |  |  |
| subjects affected / exposed   | 2 / 21 (9.52%)    |  |  |
| occurrences (all)   | 3                 |  |  |
| Ast increased   |                   |  |  |
| subjects affected / exposed   | 2 / 21 (9.52%)    |  |  |
| occurrences (all)   | 4                 |  |  |
| Weight decreased  |                   |  |  |
| subjects affected / exposed   | 2 / 21 (9.52%)    |  |  |
| occurrences (all)   | 2                 |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |  |  |
| Tumour pain   |                   |  |  |
| subjects affected / exposed   | 2 / 21 (9.52%)    |  |  |
| occurrences (all)   | 3                 |  |  |
| Nervous system disorders  |                   |  |  |
| Neuropathy peripheral   |                   |  |  |
| subjects affected / exposed   | 9 / 21 (42.86%)   |  |  |
| occurrences (all)   | 39                |  |  |
| Blood and lymphatic system disorders                                |                   |  |  |
| Anaemia   |                   |  |  |
| subjects affected / exposed   | 3 / 21 (14.29%)   |  |  |
| occurrences (all)   | 4                 |  |  |
| Thrombocytopenia  |                   |  |  |
| subjects affected / exposed   | 3 / 21 (14.29%)   |  |  |
| occurrences (all)   | 5                 |  |  |
| General disorders and administration site conditions                |                   |  |  |
| Fatigue   |                   |  |  |
| subjects affected / exposed   | 18 / 21 (85.71%)  |  |  |
| occurrences (all)   | 59                |  |  |
| Pyrexia   |                   |  |  |
| subjects affected / exposed   | 5 / 21 (23.81%)   |  |  |
| occurrences (all)   | 5                 |  |  |
| Gastrointestinal disorders  |                   |  |  |



|   |                        |  |  |
|---|------------------------|--|--|
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)  | 2 / 21 (9.52%)<br>2    |  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)  | 11 / 21 (52.38%)<br>24 |  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 5 / 21 (23.81%)<br>9   |  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 6 / 21 (28.57%)<br>13  |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 13 / 21 (61.90%)<br>23 |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 6 / 21 (28.57%)<br>9   |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)      | 3 / 21 (14.29%)<br>3   |  |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)   | 2 / 21 (9.52%)<br>2    |  |  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all)            | 4 / 21 (19.05%)<br>14  |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 4 / 21 (19.05%)<br>5   |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 2 / 21 (9.52%)<br>6    |  |  |

|  |                       |  |  |
|--|-----------------------|--|--|
| Bone pain<br>subjects affected / exposed<br>occurrences (all)  | 3 / 21 (14.29%)<br>4  |  |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)  | 5 / 21 (23.81%)<br>11 |  |  |
| Infections and infestations<br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>2   |  |  |
| Metabolism and nutrition disorders<br>Anorexia<br>subjects affected / exposed<br>occurrences (all)         | 8 / 21 (38.10%)<br>20 |  |  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 21 (9.52%)<br>3   |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

The threshold for proving antitumor activity (at least nine patients reaching PFS4) was not reached, the primary endpoint was unmet, and the study was closed without recruiting more patients in the first stage and without opening the second stage

Notes: