



Clinical trial results:

A Phase II, Open-label, Multicenter Study of PM060184 in Patients with Advanced Colorectal Cancer after Standard Treatment

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-000257-39 |
| Trial protocol | ES |
| Global end of trial date | 11 February 2019 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 31 October 2020 |
| First version publication date | 31 October 2020 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | PM60184-B-002-17 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03427268 |
| 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., Pharmamar, S.A., 34 91846 60 00, clinicaltrials@pharmamar.com |
| Scientific contact | Clinical Development, Department of PharmaMar's Oncology, Business Unit., Pharmamar, 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 August 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 11 February 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 February 2019 |
| 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 12 weeks (PFS3) in patients with advanced colorectal carcinoma (CRC) after standard therapy.

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 American Society of Clinical Oncology (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 in accordance with ASCO guidelines

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 16 January 2018 |
| 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: 31 |
| Country: Number of subjects enrolled | Canada: 1 |
| Worldwide total number of subjects | 32 |
| EEA total number of subjects | 31 |

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) | 23 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The first informed consent was signed on 16 January 2018 and the first study treatment administration was on 8 February 2018. The cutoff date for the results was 11 February 2019 (date of last follow-up).

Pre-assignment

Screening details:

signed CI; Age ≥ 18 years; Histologically-citologically documented adenocarcinoma of colon or rectum that had progressed to the last prior treatment before inclusion; Measurable disease according to RECIST v.1.1; Previous treatment in any setting with fluoropyrimidine, oxaliplatin and irinotecan in any combination; No more than 2 previous therapies

Period 1

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

Arms

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

Arm description:

PM060184 was administered i.v. via a central line or a peripheral venous catheter (in 30-min administration) at a dose of 9.3 mg/m² on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle) (dose can be rounded to the first decimal point).

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | PM060184 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

PM060184 was administered i.v. via a central line or a peripheral venous catheter (in 30-min administration) at a dose of 9.3 mg/m² on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle) (dose can be rounded to the first decimal point).

| Number of subjects in period 1 | PM060184 |
|---------------------------------|----------|
| Started | 32 |
| Completed | 0 |
| Not completed | 32 |
| Consent withdrawn by subject | 1 |
| Study termination | 1 |
| Never treated | 2 |
| Progressive disease | 25 |
| Treatment-related adverse event | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Overall period |
|-----------------------|----------------|

Reporting group description: -

| Reporting group values | Overall period | Total | |
|--|----------------|-------|--|
| Number of subjects | 32 | 32 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 18-49 | 4 | 4 | |
| 50-69 | 23 | 23 | |
| ≥70 | 5 | 5 | |
| Age continuous | | | |
| Units: years | | | |
| median | 62 | | |
| full range (min-max) | 36 to 74 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 17 | 17 | |
| Male | 15 | 15 | |
| Race | | | |
| Units: Subjects | | | |
| White | 32 | 32 | |
| ECOG PS | | | |
| ECOG PS, Eastern Cooperative Oncology Group performance status | | | |
| Units: Subjects | | | |
| PS 0 | 15 | 15 | |
| PS I | 17 | 17 | |
| Stage at diagnosis | | | |
| Units: Subjects | | | |
| Stage I | 1 | 1 | |
| Stage IIIB | 5 | 5 | |
| Stage IIIC | 2 | 2 | |
| Stage IV | 17 | 17 | |
| Stage IVA | 3 | 3 | |
| Stage IVB | 3 | 3 | |
| UK | 1 | 1 | |
| Primary tumor side | | | |
| Units: Subjects | | | |
| Left | 22 | 22 | |
| Right | 10 | 10 | |
| Histology grade | | | |
| Units: Subjects | | | |
| G1: Well differentiated | 8 | 8 | |
| G2: Moderately differentiated | 18 | 18 | |
| G4: Undifferentiated | 1 | 1 | |
| GX: Grade cannot be assessed | 5 | 5 | |

| | | | |
|--|---------------|----|--|
| KRAS mutation status Units: Subjects | | | |
| Mutated | 25 | 25 | |
| Not done | 6 | 6 | |
| UK | 1 | 1 | |
| Sites involved Units: Subjects | | | |
| 1 site | 5 | 5 | |
| 2 sites | 12 | 12 | |
| 3 sites | 8 | 8 | |
| 4 sites | 5 | 5 | |
| 6 sites | 1 | 1 | |
| 7 sites | 1 | 1 | |
| Peripheral neuropathy Units: Subjects | | | |
| Yes | 19 | 19 | |
| No | 13 | 13 | |
| Prior surgery Units: Subjects | | | |
| Yes | 28 | 28 | |
| No | 4 | 4 | |
| Prior radiotherapy Units: Subjects | | | |
| Concurrent | 1 | 1 | |
| Palliative | 4 | 4 | |
| No | 27 | 27 | |
| Prior anticancer lines Units: Subjects | | | |
| 1 line | 1 | 1 | |
| 2 lines | 26 | 26 | |
| 3 lines | 5 | 5 | |
| Best response to last prior therapy | | | |
| CR, complete response; PD, disease progression; PR, partial response; SD, stable disease; UK,unknown | | | |
| Units: Subjects | | | |
| CR | 2 | 2 | |
| PR | 3 | 3 | |
| SD | 14 | 14 | |
| PD | 9 | 9 | |
| UK | 4 | 4 | |
| Weight Units: Kg | | | |
| median | 67 | | |
| full range (min-max) | 39.6 to 105.5 | - | |
| Height Units: cm | | | |
| median | 166 | | |
| full range (min-max) | 150 to 183 | - | |
| Body surface area Units: m^2 | | | |
| median | 1.8 | | |
| full range (min-max) | 1.3 to 2.3 | - | |

| | | | |
|---|---------------------|---|--|
| Time from diagnosis of advanced disease to study entry Units: months median full range (min-max) | 17.3 5.8 to 69.5 | - | |
| Time from first diagnosis to first PM060184 infusion Units: months median full range (min-max) | 22.9 7.9 to 57.1 | - | |
| Time from prior last progression before study entry Units: months median full range (min-max) | 1.2 0 to 3.2 | - | |
| Time from stop date of prior chemotherapy to study entry Units: months median full range (min-max) | 1.8 0.1 to 6.3 | - | |
| Sites involved Units: sites median full range (min-max) | 2 1 to 7 | - | |
| Prior anticancer lines Units: lines median full range (min-max) | 2 1 to 3 | - | |

End points

End points reporting groups

| | |
|---|----------|
| Reporting group title | PM060184 |
| Reporting group description: PM060184 was administered i.v. via a central line or a peripheral venous catheter (in 30-min administration) at a dose of 9.3 mg/m ² on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle) (dose can be rounded to the first decimal point). | |

Primary: Progression-free survival rate at three months

| | |
|---|---|
| End point title | Progression-free survival rate at three months ^[1] |
| End point description: Progression-free survival rate at 12 weeks (PFS3), defined as the rate estimate of the percentage of patients who are alive and progression-free at 12 weeks (~3 months) after the first treatment administration. | |
| End point type | Primary |
| End point timeframe: Time from the first day of study treatment to the day of assessment of progression, death or last tumor evaluation, up to 3 months | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: The exact binomial estimator and its 95% confidence interval (CI) were used for the primary endpoint (PFS3) | |

| | | | | |
|-----------------------------------|-------------------|--|--|--|
| End point values | PM060184 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 ^[2] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 20.7 (8 to 39.7) | | | |

Notes:
[2] - 2 patients were never treated
1 treated patient not receive 2 administrations over 2 cycles

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|--|------------------|
| End point title | Overall Survival |
| End point description: Events 15 (51.7%) 999, not reached | |
| End point type | Secondary |
| End point timeframe: From the first day of treatment to the date of death or last contact | |

| | | | | |
|----------------------------------|-------------------|--|--|--|
| End point values | PM060184 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 ^[3] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9.8 (4.6 to 999) | | | |

Notes:

[3] - 2 patients were never treated

1 treated patient not receive 2 administrations over 2 cycles

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival

| | |
|-----------------|---------------------------|
| End point title | Progression-free Survival |
|-----------------|---------------------------|

End point description:

Progression-free survival (PFS), defined as the time from the first day of study treatment to the day of assessment of progression, death or last tumor evaluation

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

End point timeframe:

Time from the first day of study treatment to the day of assessment of progression, death or last tumor evaluation

| | | | | |
|----------------------------------|-------------------|--|--|--|
| End point values | PM060184 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 ^[4] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 2.6 (1.3 to 2.8) | | | |

Notes:

[4] - 2 patients were never treated

1 treated patient not receive 2 administrations over 2 cycles

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival at 3 months

| | |
|-----------------|---------------------------------------|
| End point title | Progression-free Survival at 3 months |
|-----------------|---------------------------------------|

End point description:

Progression-free survival (PFS), defined as the time from the first day of study treatment to the day of assessment of progression, death or last tumor evaluation

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

End point timeframe:

Time from the first day of study treatment to the day of assessment of progression, death or last tumor evaluation, up to 3 months

| | | | | |
|-----------------------------------|--------------------|--|--|--|
| End point values | PM060184 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 ^[5] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 25.3 (9.1 to 41.4) | | | |

Notes:

[5] - 2 patients were never treated

1 treated patient not receive 2 administrations over 2 cycles

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate

| | |
|-----------------|-----------------------|
| End point title | Overall Response Rate |
|-----------------|-----------------------|

End point description:

Overall Response Rate defined as the percentage of patients with either complete response (CR) or partial response (PR) according to RECIST v.1.1.

PD, disease progression; SD, stable disease; RECIST, Response Evaluation Criteria in Solid Tumors

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

End point timeframe:

Overall period

| | | | | |
|-----------------------------|-------------------|--|--|--|
| End point values | PM060184 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 ^[6] | | | |
| Units: subjects | | | | |
| SD <3 months | 9 | | | |
| SD ≥3 months | 7 | | | |
| PD | 13 | | | |

Notes:

[6] - 2 patients were never treated

1 treated patient not receive 2 administrations over 2 cycles

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 | 20.0 |
|--------------------|------|

Reporting groups

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

Reporting group description:

PM060184 was administered i.v. via a central line or a peripheral venous catheter (in 30-min administration) at a dose of 9.3 mg/m² on Day 1 and Day 8 every three weeks (q3wk) (three weeks = one treatment cycle) (dose can be rounded to the first decimal point).

| Serious adverse events | PM060184 | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | | |
| number of deaths (all causes) | 16 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|-------------------|--|--|
| Non-serious adverse events | PM060184 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 30 (100.00%) | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Aspartate aminotransferase increased | | | |

| | | | |
|-------------------------------------|-----------------|--|--|
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 5 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Weight decreased | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 7 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 7 | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 9 | | |
| Nervous system disorders | | | |
| Dysaesthesia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 10 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 4 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 9 | | |
| Neurotoxicity | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 7 | | |
| Paraesthesia | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Peripheral sensory neuropathy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>14 / 30 (46.67%)</p> <p>52</p> <p>3 / 30 (10.00%)</p> <p>12</p> | | |
| <p>Blood and lymphatic system disorders</p> <p>Anaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neutropenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 30 (23.33%)</p> <p>14</p> <p>3 / 30 (10.00%)</p> <p>3</p> | | |
| <p>General disorders and administration site conditions</p> <p>Asthenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Chest pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>22 / 30 (73.33%)</p> <p>74</p> <p>2 / 30 (6.67%)</p> <p>4</p> <p>5 / 30 (16.67%)</p> <p>10</p> | | |
| <p>Gastrointestinal disorders</p> <p>Abdominal distension</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Abdominal pain upper</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Constipation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> | <p>2 / 30 (6.67%)</p> <p>2</p> <p>20 / 30 (66.67%)</p> <p>66</p> <p>5 / 30 (16.67%)</p> <p>15</p> <p>19 / 30 (63.33%)</p> <p>61</p> | | |

| | | | |
|---|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 11 / 30 (36.67%) 33 | | |
| Nausea subjects affected / exposed occurrences (all) | 9 / 30 (30.00%) 23 | | |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 7 | | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 14 / 30 (46.67%) 54 | | |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 11 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 7 | | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 9 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 5 / 30 (16.67%) 13 | | |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 6 | | |
| Infections and infestations Device related infection subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 3 | | |
| Metabolism and nutrition disorders Decreased appetite | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 10 / 30 (33.33%) | | |
| occurrences (all) | 26 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 27 July 2017 | <p>The main objective of this amendment was to change the infusion time of PM060184 from 1 minute to 30 minutes. This was decided following the analysis of preliminary data from the phase II trial PM60184-B-001-15 in hormone receptor-positive, HER2-negative, advanced breast cancer patients, which evaluated short infusion times (one and five minutes) to simplify PM060184 administration. Preliminary safety data from this trial suggest that the overall toxicity profile of PM060184 administered at shorter infusion times (one minute and five minutes) was similar to that observed in 104 patients treated with single-agent PM060184 at different doses during phase I trials. However, it seems that the higher maximum plasma concentration (C_{max}) of shorter infusion times was associated with an increased incidence of adverse events at the dose of 9.3 mg/m². In addition, results from the phase I trial PM60184-A-002a-10, which evaluated the same schedule but at an infusion of 10 minutes, showed that at the recommended dose (RD) of 9.3 mg/m² five patients had Day 8 infusion omissions, but in only one case the omission was due to drug-related toxicity (grade 2 neutropenia). Thus, the relative dose intensity was 91.3%. Furthermore, due to its limited solubility, PM060184 must be administered in a very low volume by means of a syringe pump. This device's performance is highly affected by the system's pressure, which in turn depends on the duration of the infusion. Thus, the longer the infusion, the fewer chances of device malfunction. Besides, longer infusion times are more convenient for reliable characterization of pharmacokinetic (PK) parameters, especially maximum plasma concentration (C_{max}), since these parameters are not affected by variability at the collection window around the end of infusion as much as in shorter infusions. In accordance with these considerations, the infusion time of PM060184 was changed to 30 minutes and the reconstitution guidelines were updated.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported